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CHILDHOOD OBESITY TREATMENT: INTEGRATING MOBILE HEALTH TECHNOLOGY INTO A PAEDIATRIC OBESITY SERVICE

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This dissertation is submitted for the degree of Ph.D.
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January 2015

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CONTENTS

1 INTRODUCTION 1

1.1 Aetiology of obesity 1

1.2 Obesity and associated co-morbidity 2

1.3 Reducing the burden of obesity 3

1.4 Childhood obesity treatment in Ireland 5

1.5 Ph.D. overview 5

1.6 Publications 7

2 LIFESTYLE TREATMENT OF CHILDHOOD OBESITY: A SYSTEMATIC REVIEW 10

2.1 Part A- Face-to-face interventions: Abstract 11

2.2 Part A: Background 12

2.3 Part A: Aim 12

2.4 Part A: Method 12

2.5 Part A: Results 15

2.6 Part A: Discussion 20

2.7 Part A: Conclusion 27

2.8 Part B mHealth interventions: Abstract 29

2.9 Part B mHealth interventions: Background 30

2.10 Part B mHealth interventions: Aim 32

2.11 Part B mHealth interventions: Method 32

2.12 Part B mHealth interventions: Results 34

2.13 Part B mHealth interventions: Discussion 38

2.14 Part B mHealth interventions: Conclusion 43

2.15 Acknowledgements 43

3 CARDIOMETABOLIC CO-MORBIDITY IN CHILDHOOD OBESITY 60

3.1 Abstract 61

3.2 Background 63

3.3 Aims 63

3.4 Methods 64

3.5 Results 68

3.6 Discussion 72

3.7 Conclusion 75

3.8 Acknowledgements 75

4 THE ROLE OF BODY COMPOSITION: DOES CHANGE PREDICT METABOLIC FUNCTION? 79

4.1 Abstract 80

4.2 Background 82

4.3 Aim 83

4.4 Methods 83

4.5 Results 84

4.6 Discussion 89

4.7 W82GO evaluation: conclusion 92

4.8 Acknowledgements 92

5 W82GO HEALTHY LIFESTYLES SERVICE: DEVELOPMENT AND CLINCAL EFFECT OF A CHILDHOOD OBESITY INTERVENTION 98

5.1 Abstract 99

5.2 W82GO development: background 101

5.3 W82GO development: aim 101

5.4 W82GO development: methods 102

5.5 W82GO development: results 111

5.6 W82GO development: conclusion 111

5.7 W82GO development acknowledgements 111

5.8 W82GO evaluation: background 113

5.9 W82GO evaluation: aims 113

5.10 W82GO evaluation: method 113

5.11 W82GO evaluation: results 116

5.12 W82GO evaluation: discussion 119

5.13 W82GO evaluation: conclusion 122

5.14 W82GO evaluation acknowledgements 122

6 DEVELOPMENT AND TESTING OF A SMARTPHONE APPLICATION FOR OBESITY MANAGEMENT 128

6.1 Abstract 129

6.2 Part A: background to development 131

6.3 Part A: aim of development 133

6.4 Part A: methods of development 133

6.5 Part A: results of development 139

6.6 Part A: discussion 149

6.7 Part A: Conclusions 150

6.8 Part A: Acknowledgements 150

6.9 Part B: background to usability testing 150

6.10 Part B: methods of usability testing 152

6.11 Part B: results of usability testing 155

6.12 Part B: discussion 156

6.13 Part B: conclusions 159

6.14 Acknowledgements 159

7 MHEALTH INTERVENTION IN ADOLESCENT OBESITY: A MID-POINT REPORT 162

7.1 Abstract 163

7.2 Background 164

7.3 Aim 164

7.4 Methods 164

7.5 Results 169

7.6 Discussion 172

7.7 Conclusion 177

7.8 Acknowledgements 177

8 DISCUSSION 182

8.1 Summary of findings 182

8.2 Strengths and Limitations 185

8.3 Implications of findings 190

8.4 Implications specific to mHealth interventions 193

8.5 Recommendations for further research 194

9 CONCLUSION 197

10 REFERENCES 199

DECLARATION

This dissertation is the result of my own work and includes nothing, which is the outcome of work done in collaboration except where specifically indicated in the text. It has not been previously submitted, in part or whole, to University College Cork or to any university of institution for any degree, diploma, or other qualification.

Signed: _____

Date: _____

Grace O'Malley M.Sc. B.Sc. (Hons.) M.I.S.C.P.

University College Cork.

This work is dedicated to my parents and family. Tom and Breege O'Malley have shown me that an inquisitive mind guided by compassion and empathy is a most powerful tool for achieving change. I could never have started this work, nor could I continue it, without the encouragement, love and support of Tom, Breege, my husband Richard Lambe, my sister Karina, my brothers (Anthony and Cathal) and all of my friends.

PERSONAL STATEMENT

This thesis is the culmination of ten years of clinical practice and research experience in the area of paediatric obesity management. I am often asked how I, as a physiotherapist, ended up working in the area of childhood weight management. As such, the following functions as a brief overview to set the scene regarding my involvement in this highly topical area. I first commenced working as a chartered physiotherapist in the orthopaedic outpatients in Temple Street Children's University Hospital. During this time, I was surprised by the number of children who were overweight and who were presenting with a variety of musculoskeletal conditions that appeared to be solely due to their lack of physical conditioning. In order to explore this hypothesis I began to collect standardised data regarding the musculoskeletal health of children who were overweight and obese. In addition, I registered for a master's degree in research under the guidance of Dr. Juliette Hussey in the school of physiotherapy, Trinity College. Throughout the M.Sc., I gained further insight into the biomechanical effects of childhood obesity and published work describing the lower limb musculoskeletal impairments in a small group of children attending Dr. Edna Roche's weight management service at the National Children's Hospital in Tallaght. In addition, I began to work with a number of clinical colleagues in Temple Street in order to establish an outpatient's service (the Streeetwise Healthy Lifestyles Programme) for children referred for weight management.

I continued to ponder the interaction between physical activity, bone health and the risk of fractures and was delighted to spend a short period of time investigating these links during a research residency with Professor Heather McKay at the Centre for Hip Health in the University of British Columbia, Vancouver, Canada. A highlight of this residency was seeing how a multidisciplinary approach to research could result in novel world-class outputs. At this time, I was successful in my application to the Fulbright Commission and planned to explore the association between physical fitness

and mitochondrial function in children who were obese at the Yale University School of Medicine, under the mentorship of Professor Sonia Caprio. Throughout my time at Yale, I was exposed to the daily realities of conducting cutting-edge clinical research in the area of paediatrics and I was blessed to be part of a superb team who were committed to understanding the effects of ectopic fat and the pathophysiology of type-2 diabetes in youth. I also ran the exercise component of the Bright Bodies weight management programme under the mentorship of Mary Savoye and Melissa Shaw. Through Bright Bodies I gained further experience working as part of a weight management team and witnessed the daily realities of a diverse group of children who were obese. I began to understand how poverty, the economic system, social inequality, emotional health and discrimination were all linked to obesity and that tackling obesity effectively could only occur with a true multidisciplinary and cross-sectoral approach. In addition, I wondered whether scaling up clinical approaches to obesity management would ever be possible and began to sketch a plan for how a smartphone application for weight management might work. I also wondered whether my research energies should concentrate on investigating the role of behavioural economics in obesity prevention so that policy changes could attempt to prevent the development of obesity.

Upon my return to Dublin, I recommenced working in Temple Street and started to ramp up our efforts to provide an appropriate outpatient service to children who were obese. In an effort to continue researching in the area, I reduced my clinical hours to a half-time post and began a Cochrane systematic review of incentive-based approaches to increasing physical activity and fitness. In addition, I nurtured previous ideas of developing a smartphone application and was lucky to meet Prof. Ivan Perry at a research meeting in Our Lady's Hospital for Sick Children in Crumlin. Ivan encouraged me to register for a Ph.D. fellowship with the HRB in order to further nurture my idea for a smartphone application. Through the HRB application process I was acquainted with Prof. Amanda Burls and Prof. Mike Clarke and as a team we started work on developing an application

and establishing a clinical trial to test its effect.

The past four years have been extremely exciting. As mobile technology has become rooted into the public consciousness, I have witnessed the changing attitudes towards the use of these tools in healthcare (mHealth). At the beginning of this work, my proposed research was met with confusion as many of my clinical colleagues considered it to be a waste of time, funding and effort. I was encouraged to continue by my patients and no more so than by a teenager attending our weight management service who commented:

> *"Using a phone to treat fellas like me.... that's a good idea. Sure teenagers are using their phones so much that if you try to talk to one now you would be looking at the top of their head! It makes sense to try to speak to them through their phone as well."*

In the past year however, the areas of telehealth, connected health and mobile health have grown significantly and there is growing interest in using technological tools to improve the delivery of healthcare. Such tools are vital components of a healthcare system, which is grossly unprepared to deal with the huge burden of chronic disease. Throughout my Ph.D. I have tried to balance my clinical and research responsibilities and though the research has been limited by many factors I can state three things with confidence. Firstly, as a society I believe we have a duty to protect the most vulnerable amongst us and as such, children who are obese should have access to care like any other child suffering a condition which threatens his/her health. Secondly, providing effective treatment for children who are obese will require true multidisciplinary work and given the task at hand there can be little room for ego or 'fiefdom' politics. Finally, children will continue to become obese if we fail as a community to protect them. Their healthy growth and development cannot be assured without rigorous evaluation of the known and unknown factors driving obesity. Similarly, as citizens, scientists, clinicians and taxpayers we each play a role in advocating for policy changes that facilitate and empower our society to be healthier.

ACKNOWLEDGEMENTS

I would firstly like to thank sincerely the Health Research Board and the Children's Fund for Health. Without their financial support this Ph.D. would not have been possible. The Health Professionals Fellowship is a funding stream, which is vital to practicing clinicians. Without such grants it would be impossible for clinicians like myself to generate and implement research around key scientific questions related to practice.

Without the participation of the children and families recruited, this thesis would not have been possible. I heartily thank all the children and their parents who took part in this work. Their bravery in coming forward to seek healthcare for a condition, which is all too often neglected, has facilitated service developments in Temple Street Children's University Hospital and elsewhere around the country.

The clinical guidance and assistance I received from Dr. Sinéad Murphy has been indispensible over the past three years. She exemplifies a committed paediatric clinician and has been a joy to work with. With her help the W82GO team continue to meet their goals and through our advocacy work we have managed to place the treatment of childhood obesity firmly on the political and clinical agenda. With a heavy sigh of relief, the team at Temple Street recently received HSE funding for a part-time temporary clinical service. This would not have been possible without Sinéad's help and support.

I greatly thank my academic supervisors, Prof. Ivan Perry, Prof. Mike Clarke and Prof. Amanda Burls for their support and unrivalled patience throughout this work. From my first meeting with Amanda Burls, I was confident that her academic expertise would be a firm support to me throughout this journey. Her interest in and curiosity regarding technology and how it can be used to improve health outcomes has been refreshing. With her guidance and wisdom it was possible for me to nurture my scientific mind without thwarting my creativity. I sincerely thank Mike

Clarke for his constant support since 2011. I was dazzled by Mike's brilliance upon our first meeting at a Cochrane training course in Dublin and our paths crossed yet again during clinical trials training in Oxford. Without Mike's clarity and wisdom I would have never dared to dip my toe into the waters of clinical trials research. His trust in my ability to anticipate and navigate trial-related problems gave me confidence and strengthened my resolve to lead the first randomised clinical trial in Temple Street. I have no doubt that his guidance will leave an indelible mark on paediatric research in the hospital.

The work in this Ph.D. would never have been possible were it not for the support of Ivan Perry. I thank Ivan from the bottom of my heart for nurturing my confidence and allowing me to develop my research skills without disregarding my clinical intuition. His encouragement has guided me along a path toward important mental processes and transformations, which have punctuated my journey through scientific research thus far. I have thoroughly enjoyed our meetings to discuss research intricacies, project plans and other topics ranging from sport to music. Ivan inspires me as a researcher and I have no doubt that healthcare and the health outcomes of many Irish citizens have been improved through his work. Without Ivan's help and counsel I could not have navigated the complex political highways or scaled the many obstacles of bureaucracy that impeded this work.

Furthermore, I am grateful to the staff of Department of Epidemiology and Public Health especially Dr. Tony Fitzgerald, Vicky Murphy and Tara O'Connell. Their help and support have been vital during my Ph.D., particularly during my travels to and from Cork. Tony has welcomed all of my statistical queries regardless of how basic they were. His humour and coffee have kept us both going while the data limitations grew along with the study participants.

I am sure that I would have made a very poor choice of software developer had it not been for the shrewd guidance of Prof. John Morrison from the UCC Department of Computer Science. His advice and interest in this work is

greatly appreciated. Similarly the support that both John and Brian Clayton offered regarding hosting of the mHealth intervention on the UCC server was a key factor in the clinical trial being established. Their pragmatic approach to solving a litany of network-related problems saved the trial from being abandoned before it had ever commenced.

I thank the current and past W82GO team for their support and assistance with this work. The initial and on-going development of the W82GO programme would not have been possible without the hard work and dedication of Anthea Savage, Dr. Aoife Brinkley, Dr. Nuala Murphy, Kizzy Moroney, Aisling Shiels, John Butler, Roisin Thurstan, Mbonisi Ncube, Fiona Ward, Marie McInerney, Carole Boylan, Fiona Boyle, and Cathy Monaghan. Each of these has played a vital role in the development of this work and has supported me to grow as a clinician and researcher. In particular, Aoife Brinkley has helped me navigate complex political obstacles, forgive myself for weaknesses (personal and research-related) and she has urged me to keep focused on our commitment to improve the delivery of healthcare to children who are often forgotten and neglected due to the ignorance of clinical practitioners and the lack of concern by policy makers.

I thank the Fulbright Commission and Prof. Sonia Caprio for the unforgettable time I spent at Yale University. This experience taught me how a world-class paediatric clinical research centre functioned. It gave me the confidence to believe that I could play a role in improving and developing paediatric research in Ireland through my attempts to treat childhood obesity from the clinical trenches.

The staff members of the physiotherapy department in Temple Street have been truly supportive of my work. A cramped work environment, inadequate clinic space and too few office desks contribute to a recipe for likely disaster! However, during my ten years in Temple Street, my fellow physiotherapists consistently surprise me with their patience and curiosity. Over the years, their support has kept me going through difficult times. Their vocation to their clinical work ensures that every child who enters the

hospital is encouraged and facilitated to reach his/her physical potential. In particular, I thank Anthea Seager for patiently proofreading this work and providing valuable feedback. I also thank Cliona Blake for her constant support and both Lorraine Connolly and Deirdre Winston for the vital role they play in scheduling (and rescheduling) patient appointments. Without their help, it would be impossible to facilitate the work and school routines of the families we treat. I acknowledge sincerely, Deirdre Sheehan, Physiotherapy Manager. With her assistance, I have been able to embark upon a personal discovery of scientific research whilst also developing my clinical skills, and in turn, endeavouring to marry the two in my daily work. Throughout this work she has been a true friend, mentor and inspiration. Through her own work as a clinician and as a manager I have been taught that every child we treat deserves the very best service and this cannot be achieved without tirelessly advocating for equality, regardless of the physical, intellectual or emotional health of the child. She has also taught me how to be kind to myself and to my colleagues in order to optimise the work environment and conquer challenges that are all too common in healthcare.

Thanks to Grainne Dowdall for her never-ending encouragement. Her visionary ideas regarding health information technology and her creative flair have assisted me throughout this work. In addition, her humour and warmth have been a constant support.

Finally, my sincere thanks are offered to Mr. Alec Blayney, Dr. Gayle Kenney and Aranzazu Bartolome from the Temple Street Research Department. Their help and support have been vital during this work and their continued efforts will strengthen the quality of paediatric research in Ireland.

LIST OF TABLES

Table 2.1 Characteristics of studies included in the systematic review of face-to-face lifestyle interventions for childhood obesity..... 44

Table 2.2 Characteristics of studies included in the systematic review of mHealth interventions for childhood obesity..... 58

Table 3.1 Prevalence of abnormal laboratory values in children attending for weight managment..... 76

Table 3.2 Anthropometric characteristics of participants attending TSCUH for weight management (n=227)..... 77

Table 3.3 Cardiometabolic characteristics of children attending TSCUH for weight management classified by level of obesity..... 78

Table 4.1 Baseline characteristics of participants included in study exploring agreement between BIA and DXA[1]methods of esimating body composition[1]..... 94

Table 4.2 Baseline and 12-month follow-up body composition measures in study measuring agreement between BIA and DXA [1]..... 95

Table 4.3 Baseline and 12-month follow up measures of insulin sensitivity in study exploring whether changes in body composition could predict changes in insulin sensitivity[1]..... 96

Table 4.4 Bivariate correlations between body composition and sensitivity in study exploring whether changes in body composition could predict changes in insulin sensitivity..... 96

Table 4.5 Association between changes in body composition and insulin sensitivity in study exploring body composition measurement in paediatric obesity[11]..... 97

Table 6.1 Educational targets addressed in the Reactivate application 141

LIST OF FIGURES

Figure 2.1 PRISMA flow diagram of study inclusion process 18

Figure 2.2 Forest plot depicting pooled treatment effect of family-based childhood obesity treatments 20

Figure 2.3 MRI images of visceral fat deposits from Kuk et al.[129] 28

Figure 2.4 PRISMA flow diagram of studies included in the review of mHealth interventions for paediatric obesity 36

Figure 2.5 Pooled treatment effect of mHealth intervention on BMI at 12-months 38

Figure 3.1 Co-morbidities associated with childhood obesity 64

Figure 3.2 Flow-chart of patients through Study 2 and Study 4 of PhD..... 66

Figure 4.1 Bland-Altman plot for agreement on percent body fat measures between DEXA and BIA methods 87

Figure 4.2 Bland-Altman plot for agreement on fat mass measures between DEXA and BIA methods 88

Figure 4.3 Bland-Altman plot for agreement on fat free mass measures between DEXA and BIA methods 89

Figure 5.1 Group exercise sessions target movement confidence and teamwork in a safe and supportive environment.....106

Figure 5.2 12-month Change in BMI SDS by age and by treatment group in children receiving W82GO obesity intervention.....117

Figure 5.3 12-month Change in BMI SDS by obesity class and treatment group in children receiving W82GO obesity intervention 118

Figure 6.1 Behavioural theory strategies used in mobile application. 134

Figure 6.2 Screenshot of secure login for clinician content management system for the Reactivate mobile application.....142

Figure 6.3 Screenshot of clinician content management system for the Reactivate mobile application 142

Figure 6.4 Reactivate mobile application icon 143

Figure 6.5 Icon for behaviour change strategy: My Progress 144

Figure 6.6 Icon for behaviour change strategy: My Groups 144

Figure 6.7 Icon for behaviour change strategy: My Goals 145

Figure 6.8 Icon for behaviour change strategy: My Tips & Surveys 145

Figure 6.9 Icon for setting goals related to physical activity 146

Figure 6.10 Icon for setting goals related to nutrition.....146

Figure 6.11 Icon for setting goals related to sleep and relaxation 147

Figure 6.12 Icon for setting goals related to environmental change.....147

Figure 6.13 Screenshot of the Reactivate mobile application home screen148

Figure 6.14 Samsung Galaxy Y smartphone 149

Figure 7.1: 12-month smartphone trial flow diagram 166

Figure 7.2 CONSORT flow diagram of mid-point report from RCT comparing Reactivate smartphone application to W82GO Healthy Lifestyle Intervention.....170

Figure 8.1 The spectres of Wi-Fi.....195

LIST OF ABBREVIATIONS AND ACRONYMS

Abbreviation	*Meaning*
AE	Adverse events
App	Application
ASAT	Subcutaneous abdominal adipose tissue
BIA	Bioelectrical impedance analysis
BMI	Body mass index
BMI SDS	Body mass standardized deviation score
BP perc	Blood pressure percentile
Chol	Cholesterol
DXA	Dual x-ray absorptiometry
FFM	Fat free mass
FI	Fasting insulin
FM	Fat mass
FPG	Fasting plasma glucose
GDP	Gross domestic product
HDL	High-density lipoprotein
HIV	Human immunodeficiency virus
HOMA-IR	The Homeostasis Model Assessment of insulin resistance
IAAT	Intra-abdominal adipose tissue
LDL	Low-density lipoprotein
mHealth	Mobile health
mmol.	Millimoles
MRI	Magnetic resonance imaging
PC	Power calculation
PF	Percent fat
SE	Standard error
TAT	Total adipose tissue
Tg/HDL	Ratio of triglyceride to high-density lipoprotein
W82GO	Temple Street W82GO Healthy Lifestyles Programme

LIST OF APPENDICES*

- Data collection tool for review of obesity interventions
- Scientific articles published as part of the Ph.D. candidature
- Conference abstracts published during the Ph.D. candidature
- Invited presentations during the Ph.D. candidature
- Related scientific articles published by the candidate
- Smartphone study information materials
- Temple Street W82GO Healthy Lifestyles Programme materials

*Provided on CD ROM enclosed.

1 INTRODUCTION

Obesity represents one of the greatest public health challenges of our time and has been described as a 'wicked problem', which requires sustained worldwide effort if its prevalence and consequences are to be checked (1). Overweight and obesity levels in childhood have doubled or tripled between the 1970s and 1990s (2) and it is estimated that more than 200 million children are either overweight of obese (3). Data suggest that some countries have observed a levelling off of childhood obesity and recent data from the Childhood Obesity Surveillance Initiative suggested that this might also be the case in Ireland (4, 5). Worryingly, prevalence rates continue to rise in low socio-economic groups and developing nations (6). In Ireland, one quarter of children are estimated to be overweight or obese (7, 8) and although childhood height has increased during Ireland's nutrition transition, childhood weight has increased disproportionally (9). Similar to global data, Irish children who are from lower socio-economic backgrounds have higher levels of obesity compared to those living with less disadvantage (10).

1.1 Aetiology of obesity

Obesity is influenced by a wide range of genetic, biological and environmental factors, but the emergence of obesity as a global epidemic is generally accepted to be due to the massive changes seen in energy intake and energy expenditure over the past 50 years (11). Such changes have been labelled obesogenic. Humans have evolved with an efficient ability to store energy in the form of adipose tissue so that survival could be assured in times of food scarcity (12) but the development of industrialised food production, consumerism and technological advances have led to increased availability and consumption of a Western diet coupled with a reduced energy expenditure (11). A Western diet is characterised by consumption of

foods that have a low glycaemic load, are high in saturated fat but low in polyunsaturated fat, have high macronutrient but low micronutrient densities, yield a net acid load, and are high in sodium but low in fibre (13, 14). High levels of sugar-consumption in the Western diet are of particular concern to public health, as they are directly linked to an increased risk of obesity and type-2 diabetes mellitus (15, 16). Indeed, recent data suggest that diabetes is more prevalent in countries where there is a high availability of sugar compared to countries with less availability (17). Further, intake of liquid sugar is associated with the development of metabolic syndrome in children (18).

It is beyond the scope of this thesis to discuss the potential drivers of obesity at length. These are described in detail elsewhere (19), but briefly data suggest that the following factors may play a role in the development of obesity: epigenetic mechanisms; infectious agents; increasing maternal age; reproductive fitness; assortive mating; sleep debt; endocrine disrupters; pharmaceutical iatrogenesis; ambient temperature; and intrauterine and intergenerational effects.

1.2 Obesity and associated co-morbidity

The consequences of being obese are not restricted to an increased risk of disease such as diabetes in adulthood. A myriad of obesity-related health complaints are also observed during childhood and adolescence including: pain and impaired physical function (20, 21); eating disorders (22); depression (23); respiratory disease (24); abnormal glucose tolerance and insulin response (25, 26) and the early development of metabolic and cardiovascular disease (27, 28). In addition, childhood obesity increases the risk of chronic diseases later in life (29, 30), which can lead to long-term morbidity and premature mortality (31). The identification of obesity as a driver of chronic non-communicable disease was highlighted in the 2010 Global Burden of Disease Study (32). Thereafter, in 2012 the World Health Organisation (considering obesity to be one of the most serious health challenges of the 21st century) published a multi-faceted Global Action Plan

to address obesity (33). Coupled with the physical and psychological co-morbidities, obesity is also identified as a major driver of economic burden whereby direct costs in Ireland represented 2.7% of the total health expenditure and both direct and indirect costs represented 0.9% of the gross domestic product for 2009. In the United States the healthcare costs associated with obesity were estimated at 190 billion dollars per year or 20.6% of the overall spend on health (34, 35). Furthermore, in Ireland direct healthcare costs are anticipated to increase to €5.4 billion by 2030 in line with projected increases in the rate of obesity (36).

1.3 Reducing the burden of obesity

Addressing obesity is a complex task which is exacerbated by the multiple levels at which it operates: from the level of an individual's biology, lifestyle behaviour and family interactions to the psychology of communities, school systems, health systems and public policy. A keystone of effective obesity prevention is multi-stakeholder collaboration, which integrates systems thinking and evidence-based strategies. Clearly, in order to promote population health, prevention of obesity should be a goal of paramount importance for local and national governments. Genuine commitment to and implementation of obesity prevention strategies are needed in order to halt the progression from overweight to obesity. However, in times of scarce resources, policy makers are often presented with a difficult choice: to fund either preventive initiatives or treatment programmes. Finding the balance between prevention and treatment of the obesity is challenging, and similarities exist between the obesity epidemic and our global experience of the HIV epidemic (37).

Throughout the 1980s and 1990s efforts were made to prevent the spread of HIV via education and interventions for behaviour change. In tandem throughout the 1990's and 2000's anti-retroviral therapies improved outcomes in those receiving treatment. More recently a three-pronged approach of prevention, treatment and care has been recommended for addressing HIV. A key factor restricting our ability to curb the global HIV

pandemic has been the delivery of prevention and treatment interventions to those most affected by the virus. Currently less than 20% of individuals at high-risk of contracting HIV have access to basic prevention interventions and less than 8% receive treatment (38). Like HIV, if obesity and its associated co-morbidities are to be adequately addressed it is likely that prevention, treatment and care will be needed in equal measure. A well-functioning fair and equitable Irish health and economic system requires prevention strategies to target the 19% of Irish children classified as overweight in tandem with treatment strategies for those already classified as obese (7). Best-practice treatment interventions should be implemented as early as possible, as evidence suggests a dose-response relationship between the duration of obesity and mortality (39). Indeed, recent data suggest that treatment of childhood obesity can reduce adult morbidity and extend life-years (40).

Treatment efficacy and effectiveness for child and adolescent obesity has been reported via systematic reviews and meta-analyses which show that sufficient evidence exists for evidence-based obesity treatment in childhood (41, 42). Effective treatment involves multi-faceted family-based lifestyle change aimed to improve nutrition and sleep, to increase physical activity and fitness and to reduce sedentary pursuits.

The healthcare sector has a role in reducing the burden of obesity through the delivery of treatment strategies. Based on the prevalence data to date, the delivery of effective treatment of youth who are obese will be a major challenge. One way of addressing this challenge might be through the use of technology and more specifically the use of mobile technologies. Systematic reviews have suggested that interactive computer-based interventions can be effective for weight management in adults who are overweight or obese as compared to no intervention or minimal intervention (43, 44). A Cochrane meta-analysis of 2,537 adults described six-month weight losses that were superior to minimal interventions but inferior to face-to-face interventions. With the advent of web-enabled mobile devices, it is

uncertain whether such portability will enhance the effect of computer-based 'telemedical' interventions or offer additional adverse consequence.

Mobile-health (mHealth) interventions have been used as therapeutic weight management strategies in adults (45-50), but data regarding the use of mHealth interventions for obesity is sparse in paediatrics. This Ph.D. focuses on the evidence-based treatment of child and adolescent obesity and the thesis explores whether mobile technologies can effectively be used in the Irish healthcare setting to augment the treatment of adolescents who are clinically obese.

1.4 Childhood obesity treatment in Ireland

In Ireland there currently exists only one intervention aimed at treating clinical obesity in children and adolescents. In 2004, the author and representatives from the Departments of Nursing, Psychology, Physiotherapy and Dietetics of Temple Street Children's University Hospital met to address the challenge of the growing number of children presenting to the hospital with clinical obesity. The outcome of that initial exercise was the development of the Temple Street W82GO Healthy Lifestyles Programme (then known at the Streetwise Programme), which was officially launched in 2013. The following chapters describe a series of studies ranging from the development and implementation of W82GO for delivery in a paediatric hospital setting, to the development of a clinician-assisted remote obesity treatment delivered via a smartphone application over a mobile phone network.

1.5 Ph.D. overview

The focus of this PhD is on the management of clinical obesity (BMI >98th centile) in children. The aims were: to review the published literature regarding lifestyle treatment of childhood obesity; to explore whether Irish children who are obese present with risks of cardiometabolic disease and whether their prevalence increases as obesity level increases; to describe

the development and clinical effectiveness of a family-based lifestyle intervention for childhood obesity; to compare the measurement of body composition using two methods and to explore the extent to which measures of body composition predict metabolic function in children who are obese. Finally the fifth aim was to develop and test a mobile health (mHealth) intervention for use in the management of adolescent obesity in a specialist tertiary referral centre.

- Following this introductory chapter, chapter two describes the current evidence for treatment of childhood obesity. Part A provides a systematic review and meta-analysis of the evidence for family-based lifestyle treatments. Part B outlines the use of technology in behaviour change interventions and systematically reviews the use of mobile-health (mHealth) interventions in child and adolescent obesity.
- Chapter three describes a cross-sectional study of the cardiometabolic risk factors identified in children attending a national obesity service.
- In line with the recommendation that childhood obesity interventions be evaluated using outcome measures such as body composition (51), chapter four describes a study exploring two methods of estimating body composition and their ability to predict changes in metabolic health. This work was undertaken with Professor Sonia Caprio at the Yale School of Medicine while the candidate was a Fulbright scholar.
- Chapter five describes the development of a family-based lifestyle intervention (W82GO) for children who are obese. Subsequently a pre-post study describes the 12-month change in body mass index (BMI) observed between a group of children treated with W82GO and a control group.
- Chapter six describes the development and usability testing of an mHealth system for use in the management of adolescent obesity.
- Chapter seven describes the protocol and preliminary data from a

randomised trial comparing the effect of the mHealth and the W82GO intervention on BMI.

- Finally, Chapter eight discusses the main findings of this body of research against the background of the current knowledge base and makes recommendations for future work in the area childhood obesity intervention.

1.6 Publications

1.6.4.1 Scientific articles published as part of the Ph.D. candidature

The following articles have been published or are in press:

- O'Malley G, Dowdall G, Clark M, Burls A, Murphy S, Perry I.J. Exploring the Usability of a Smartphone Application for Adolescent Obesity Management. JMIR mHealth 2014;2(2): e29.
- O'Malley G, Clarke M, Burls A, Murphy S, Murphy N, Perry IJ. A smartphone intervention for adolescent obesity: study protocol for a randomised controlled non-inferiority trial. Trials. 2014; 15:43.
- O'Malley G, Northrup N, Pierpont B, Shaw M, Weiss R and Caprio S. Tracking Changes in Metabolic Function with Changes in Body Composition in adolescent obesity.
- O'Malley G, Baker PRA, Francis DP, Perry IJ, Foster C. Incentive-based interventions for increasing physical activity and fitness [10.1002/14651858.CD009598]. 2012. 1. This work is on going and will not be reported in the following chapters.

The following articles are in preparation:

- O'Malley G, Clarke M, Burls A, Murphy S, Perry IJ. Development of a smartphone application for adolescent obesity.
- O'Malley G, Moroney K, McInerney M, Ward F, Killeen S, Murphy S, Perry IJ, Brinkley A. 12-month effects of the Temple Street W82GO Healthy Lifestyles Programme for paediatric obesity.
- O'Malley G, Carroll A, Killeen S, Ward F, Brinkley A, Murphy S, Perry

IJ, Cardiometabolic risk factors in children attending the temple street W82GO healthy lifestyles service.

1.6.4.2 Conference abstracts published as part of the Ph.D. candidature

- O'Malley G, Killeen S, Murphy S. Are balance and quality of life impaired in children who are obese? Appetite. 2014; 76(0):198.
- O'Malley G, Brinkley A, Moroney K, McInerney M, Murphy S, Killeen S, Murphy N. Establishing a hospital based obesity service: An Irish Experience. Obesity Facts 2012; 5(S10):9.
- O'Malley G, Brinkley A, Moroney K, McInerney M, Murphy S, Killeen S, Murphy N. Is the Temple Street W82Go Healthy Lifestyles Programme effective in reducing BMI SDS? Obesity Facts 2012; 5(S10): 223.

1.6.4.3 Related scientific articles published by the candidate

The following articles have been published or are in press:

- Holm JC, Nowicka P, Farpour-Lambert N, O'Malley G, Hassapidou M, Weiss R and Baker J. The ethics of childhood obesity treatment. Obesity Facts. 2014; 7(4): 247-281.
- Braet C, O'Malley G; Weghuber D; Nowicka P; Ardelt-Gattinger E. The assessment of eating behaviour in the absence of hunger in children who are obese: a psychological approach. A Position Paper from the European Childhood Obesity Group. Obesity Facts 2014;7(3):153-164.
- Dowdall G, O'Malley G, Barton H. Acceptability of a mobile application for adolescent obesity management: parental and child perspectives (in press).
- Landauer F, Huber G, Paulmichl K, O´Malley G, Mangge Harald, Weghuber D. Timely diagnosis of malalignment of the distal extremities is crucial in morbidly obese juveniles. Obesity Facts 2013;6(6):542-51.
- O'Malley G, Hussey J, Roche E. A pilot study to profile the lower limb

musculoskeletal health in children with obesity. Pediatr Phys Ther. 2012;24(3):292-8.

- Savoye M, Nowicka P, Shaw M, Yu S, Dziura J, Chavent G, et al. Long-term results of an obesity program in an ethnically diverse paediatric population. Pediatrics. 2011;127(3):402-10.
- O'Malley G. Aerobic exercise enhances executive function and academic achievement in sedentary, overweight children aged 7-11 years. J Physiother. 2011;57(52):255.
- O'Malley G, Santoro N, Northrup V, D'Adamo E, Shaw M, Eldrich S, *et al.* High normal fasting glucose level in obese youth: a marker for insulin resistance and beta cell dysregulation. Diabetologia. 2010; 53(53): 1199-209.
- D'Adamo E, Northrup V, Weiss R, Santoro N, Pierpont B, Savoye M, *et al.* Ethnic differences in lipoprotein subclasses in obese adolescents: importance of liver and intraabdominal fat accretion. Am J Clin Nutr. 2010;92(53):500-8.
- O'Malley G, Hussey H. Hannon-Fletcher M. Hoey H. Moving towards health. Abstracts of the 19th European Childhood Obesity Group Meeting. September 17-17, 2009. Dublin, Ireland. Int J Pediatr Obes. 2010;5 Suppl 1:4-84.

2 LIFESTYLE TREATMENT OF CHILDHOOD OBESITY: A SYSTEMATIC REVIEW

2.1 Part A- Face-to-face interventions: Abstract

Background: Evidence suggests that obesity treatment delivered during childhood reduces the burden of disease and represents a good investment for public health (54-56). A 2009 Cochrane review of childhood obesity interventions concluded that family-based combined lifestyle approaches (targeting nutrition, physical activity and behavioural change) provide meaningful reductions in obesity (41).

Aim: This study aimed to review the evidence published since the 2009 Cochrane review regarding family-based lifestyle interventions for childhood obesity and to calculate the pooled 12-month treatment effect on BMI SDS.

Methods: Guidelines as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (57) were followed. The PubMed electronic database was searched for studies published between May 2008 and June 2014. Articles that described the effectiveness of interventions designed to treat obesity in children and adolescents were included if they used a randomised controlled design, were delivered using a family-based approach, and if follow-up was of at least six months duration. 12-month changes in BMI SDS were pooled and compared using a random effects model.

Results From 989 identified titles, 39 were eligible for inclusion in the review. Study characteristics including participants, interventions, outcomes and treatment effects are described. A 12-month reduction in BMI SDS of -0.16 (-0.24, -0.07) with experimental interventions was observed though analysis revealed high statistical heterogeneity. Methodological and practical issues of family-based obesity interventions are discussed. Data suggest that compared to the 2009 Cochrane meta-analysis pooled treatment effects have increased slightly.

Conclusions: Family-based lifestyle interventions can significantly reduce obesity at 12-months.

2.2 Part A: Background

The treatment of obesity is a priority for policy makers, health service workers and the general public. Clinical guidelines recommend timely treatment in order to prevent associated chronic disease, to reduce healthcare costs, and to improve health and quality of life (58). Evidence suggests that treatment delivered during childhood reduces the burden of adult disease and represents a good investment for public health (54-56) however there is no consensus regarding the timing or type of interventions needed for optimal treatment outcome. Multiple interventions for treating childhood obesity exist including: once-off education sessions in the primary care setting; school-based interventions; traditional outpatient clinic visits; inpatient programmes; weight-loss camps; pharmacotherapy; bariatric surgery and group-based multifaceted interventions targeting behaviour change.

A 2009 Cochrane review and meta-analysis of childhood obesity interventions concluded that family-based combined lifestyle approaches (targeting nutrition, physical activity and behavioural change) provide meaningful reductions in obesity (41). Since the Cochrane review was published there has been an increase in the volume of scientific literature related to childhood obesity. For example, the number of childhood obesity-related articles published in the PubMed database doubled between January 2009 and January 2014 (from 3,663 to 7,453). As such, an update to the Cochrane review is warranted.

2.3 Part A: Aim

This systematic review aimed to identify and describe the recent evidence from randomised controlled trials for the family-based lifestyle treatment of child and adolescent obesity.

2.4 Part A: Method

This review was conducted in line with the PRISMA guideline (59) and

recommendations of the Cochrane Collaboration.

2.4.1 Study design

Studies were eligible for inclusion if they met the following criteria:

- Study described a randomised controlled clinical trial of an intervention designed to treat obesity;
- Study was written in English;
- Study recruited community-dwelling children and adolescents (0-17 years) who were overweight or obese (described using standard objective methods BMI cut-offs or percent overweight);
- Intervention addressed lifestyle change (nutrition, physical activity and behaviour change) and was delivered using a family-based approach (delivered to the child plus one or more parents or family members);
- Study specified body mass index (BMI), BMI standardised deviation score (BMI SDS) or BMI percentile as a primary outcome measure;
- Follow up data was reported at least six-months post baseline measurement.

Studies were excluded if participants were identified as having an additional medical diagnosis (e.g. type-2 diabetes or Prader-Willi syndrome). Studies describing school-based, inpatient, surgical or pharmacotherapy interventions were also excluded. Similarly, studies employing a mobile-health or telemedical approach were excluded as part two of this chapter reviews this evidence separately.

2.4.2 Information sources

The PubMed electronic database was searched for studies published between May 1st 2008 (the terminal search date for the Cochrane review) and June 30th 2014. In addition the reference list of retrieved studies were searched for potentially relevant studies.

2.4.3 Search

The search terms used were:

- Child OR adolescen* AND
- Obesity OR obes* AND
- Treat* OR interven*

Filter limiters were used to identify clinical trials conducted in humans only and published in English.

2.4.4 Study selection

Titles identified during the search procedure were screened by the candidate for relevance and those that did not meet the eligibility criteria were excluded. Relevant abstracts were imported into Endnote bibliographic software (Endnote 7.0, Thomson-Reuters, New York) and abstracts were screened using a data collection tool (Appendix I).

2.4.5 Data collection

The full-text papers of eligible abstracts were reviewed and data related to study participants, study design, control group, attrition, intervention components, underlying theory, outcomes, and treatment effect were collated. In addition, data that may have increased the risk of bias were noted (e.g. randomisation and allocation methods used, validity of outcome measures, incomplete data, selective outcome reporting, group differences at baseline, protection against contamination and publication bias).

2.4.6 Data analysis

Data from eligible studies was entered into RevMan software (version 5.2.1) and the 12-month mean changes and standard deviations of BMI SDS were pooled using a random effects model. If the data in a study was reported as baseline mean and 95% confidence intervals, the mean change and standard deviations were calculated using methods recommended by the Cochrane

Collaboration (60). A forest plot of the weighted pooled effects and the associated statistical heterogeneity was calculated using RevMan.

2.5 Part A: Results

Searching the PubMed database identified 989 potential studies. After screening the titles for eligibility, 125 studies were included for further assessment. Thirty-nine studies met the criteria for inclusion in the review and 15 studies reported 12-month BMI SDS data and were included in the meta-analysis. Figure 2.1 details the reasons that studies were excluded from the review using a PRISMA flow diagram.

2.5.1 Participants of included studies

Thirty-two (61-92) of the reviewed studies recruited children between 5- and 12 years of age while seventeen studies recruited children and adolescents over 12 years (67, 70, 74-77, 80, 83, 85-87, 93-97). Only four studies were undertaken with participants under five years of age (89, 91, 98, 99). Most studies recruited children classified as overweight or obese but the definitions used to describe these terms were inconsistent across studies. Fifteen studies were undertaken with a group of children who were defined as obese (67, 72, 73, 75, 78, 79, 83-85, 89, 90, 92, 93, 99) and for most studies the North American obesity cut-off of BMI >95th centile was used. The characteristics of individual studies included in the review are described in Table 2.1.

2.5.2 Study design of included studies

All studies included in the review were randomised and controlled though only 40% of studies provided details regarding allocation concealment or methods of randomisation. Eleven of the studies (28%) allocated participants to a waiting list control groups in which they received no treatment, 12 studies (31%) utilised a usual-care control group and the remaining studies utilised an active treatment comparator group. Studies recruited between 18 and 288 participants and power calculations were

reported in most studies. Under powering was an issue highlighted in the 2009 Cochrane review where only 28% of lifestyle intervention studies detailed a power calculation.

Sixty-five percent of studies included in this review reported power calculations whereby the minimum number of trial participants was 40. Attrition varied widely across included studies and dropout rates ranged from 2%-60%. Many studies did not report how missing data were handled and an intention-to-treat analysis was used in 35% of studies. In 30% of studies repeated measures testing was used and the remained 35% used regression analysis, t-tests or chi-squared tests for proportions. Adjustment for confounders such as age, gender and baseline level of obesity was inconsistent across studies.

2.5.3 Interventions used by included studies

All of the studies included in the review integrated some form of education for participants in the areas of nutrition, physical activity and behaviour change. Interestingly, although studies were described as having behaviour change as a key component, one third of the studies reviewed failed to give any detail regarding the theory of behaviour change used to guide development of the intervention (64, 70, 72, 74, 75, 77, 79, 80, 86, 87, 92, 95, 97). Studies that did detail the underlying theory for their intervention cited the following models and theories: the transtheoretical model (62); cognitive behavioural therapy (63, 94); social cognitive theory (66, 68, 84, 90, 99); the health-belief model (67, 71, 81) or a combination of these (65, 69, 73, 76, 78, 82, 83, 89, 91, 93, 96, 98).

Intervention components included education and goal setting to: eat breakfast everyday; to increase consumption of fruit and vegetables; to reduce intake of sugar-sweetened beverages; to reduce portion sizes; to increase water intake; to increase physical activity; to reduce sedentary behaviour and to reduce the speed of eating. A number of studies integrated additional treatment tools such as the use of pedometers for increasing

physical activity level (77, 94), the provision of vegetables and meal replacements during the intervention (93, 99) and the use of a device to retrain eating behaviour by increasing the time taken to eat food (75). Practical sessions were included for physical activity in 18 studies and the majority of interventions used goal setting, self-monitoring, stimulus control and positive reinforcement as strategies to facilitate behaviour change.

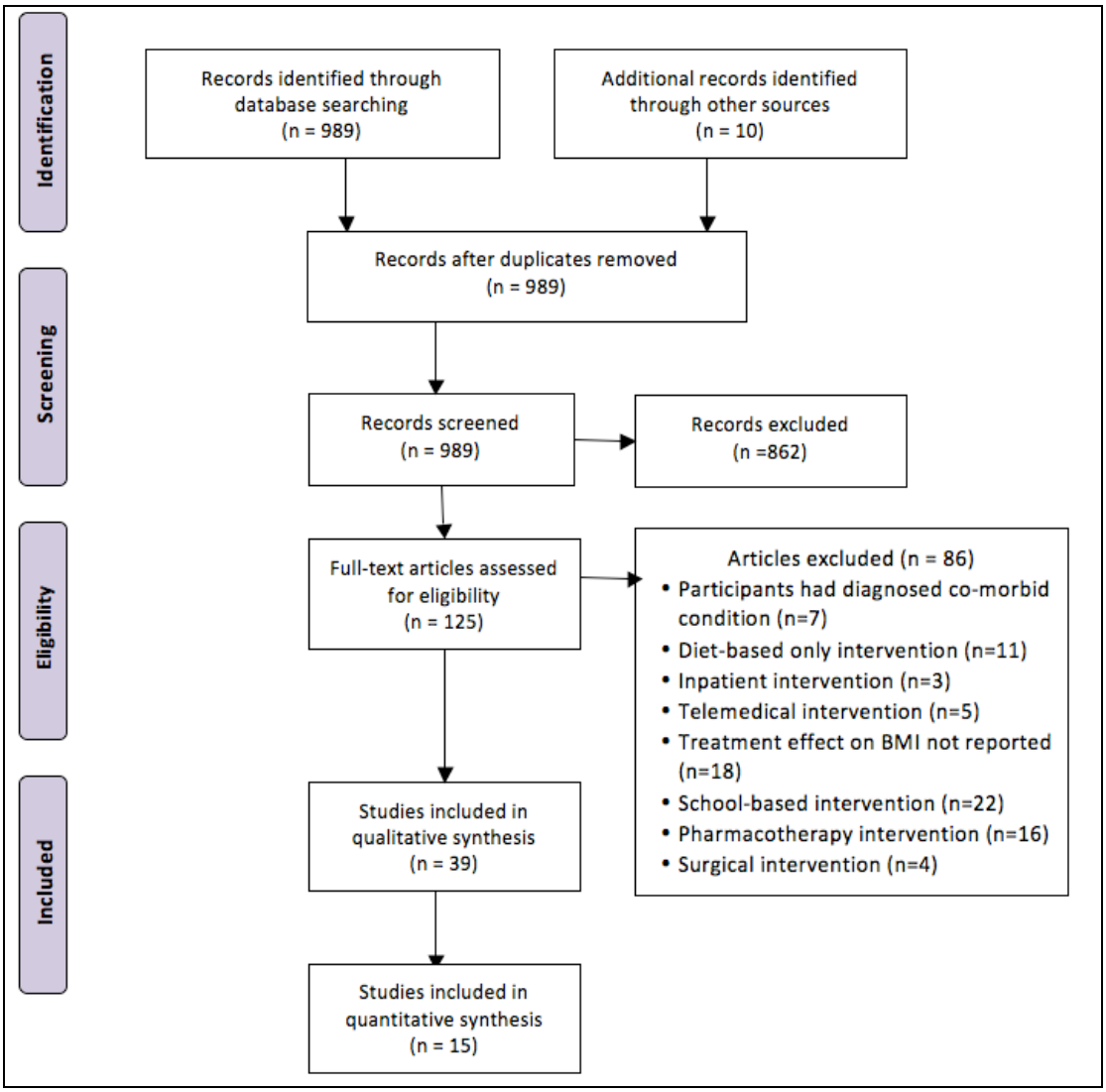
There was a high level of methodological heterogeneity among included studies as interventions varied regarding the setting in which they were delivered, the staff who delivered the treatment, the frequency of visits and whether children and parents were seen concurrently or in separate sessions. Similarly, studies varied with regard to whether participants were treated in-group sessions or individually. The characteristics of individual interventions are described in Table 2.1.

2.5.4 Outcome measures of included studies

All the studies included in this review used BMI or its derivatives as a primary outcome measure. Additional outcomes used in the studies included behavioural measures (e.g. minutes of physical activity per day, time spent in sedentary behaviour or eating behaviour), laboratory measures (e.g. insulin sensitivity or cholesterol), health-related quality of life measures and measures of psychosocial health and wellbeing. Only four studies included financial cost as an outcome (70, 76, 88, 96).

Six studies (73, 75, 82, 84, 91, 96) reported that adverse events were monitored during the intervention. Adverse events such as impaired linear growth, the development of eating disorders and negative effects on psychological well-being have been previously reported in childhood obesity trials however the studies above reported that no adverse events were observed during the study periods.

Figure 2.1 PRISMA flow diagram of study inclusion process



2.5.5 Treatment effect of included studies

2.5.4.1 Treatment effect at 6-months

This review included trials that had follow-up data of at least a 6-month duration. Three studies reported non-significant 6-month changes in obesity with intervention. These studies were undertaken with children under 12 years. The first study compared screening for obesity followed by brief counselling against an information letter and reported a treatment effect of -0.12 ($p>0.05$)(88). The second compared a group intervention (208 contact hours) aimed to improve nutrition and increase activity against a waiting list control and described a statistically insignificant change in BMI

SDS of -0.09 (p>0.05) (90). The third study compared a group treatment (9 contact hours) specifically designed for Latino families against a waiting list control and observed a change in BMI SDS of -0.03 (p>0.05) in the intervention group (61).

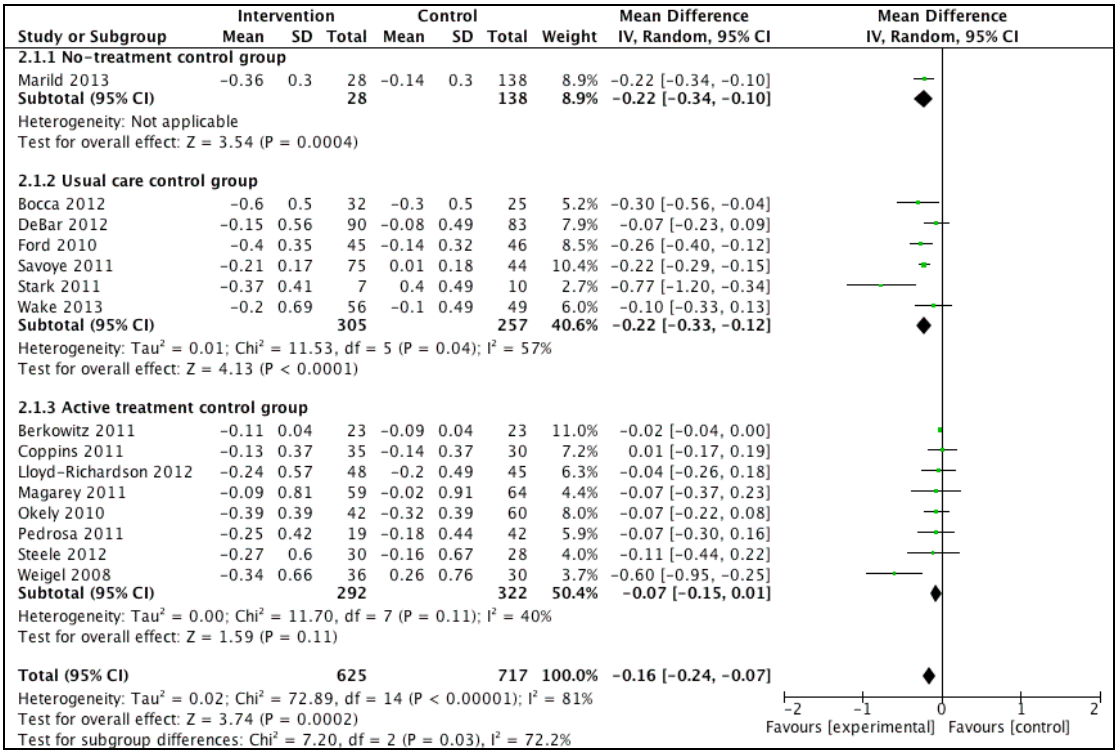
Nine other studies reported 6-month changes in BMI, which favoured intervention over control. For those studies comparing an intervention to a no-treatment waiting list control, statistically significant treatment effects on BMI SDS were observed by Sacher *et al.* (-0.24, p<0.001)(84), by Reinehr *et al.* (-0.27, p<0.001)(96) and by Croker *et al.* (-0.10, p<0.05)(73). Six studies compared an intervention against 'usual care' and statistically significant treatment effects on BMI SDS were observed by Weigel *et al.* (-0.22, p<0.05)(87); Stark *et al.* (-0.59, p<0.003)(99), by Savoye *et al.* (-0.17, p<0.001)(85), by Pedrosa *et al.* (-0.13, p<0.05)(92) and by Diaz *et al.* (-0.26, p<0.05)(67).

2.5.4.2 Meta-analysis of treatment effect at 12-months

A total of 15 studies reported 12-month BMI SDS follow-up data and were included in the meta-analysis. The total sample of participants equalled 1342 children and adolescents with 625 allocated to experimental condition and 717 allocated to control. An overall BMI SDS pooled effect of -0.16 (-0.24, -0.07) was observed for experimental interventions (p=0.0002) at 12-month follow up. Fig 2.2 depicts the meta-analysis forest plot. This improvement in BMI SDS is more than the minimal clinically meaningful change observed in a Norwegian study but less than that described in studies from the UK and Germany (100-102). Kolsgaard *et al.* observed a reduction in BMI SDS of 0.1 was associated with improved cardiovascular profile however studies by Ford *et al.* (101) and Reinehr *et al.* (102) observed that a reduction of at least 0.25 was required to benefit cardiometabolic health. Results of the meta-analysis revealed that there was a high level of statistical heterogeneity observed, where the chi–square test was significant, the chi-square statistic was higher than the degrees of freedom (72.89) and the I^2 value was 81%. As such the results of the meta-

analysis should be considered with caution.

Figure 2.2 Forest plot depicting pooled treatment effect of family-based childhood obesity treatments



2.6 Part A: Discussion

This study aimed to review the evidence regarding the treatment of child and adolescent obesity using family-based lifestyle interventions. On the whole, studies used heterogeneous study designs and interventions. The participants recruited to the studies were mainly children under 12 years and compared to the 2009 Cochrane a greater number of studies recruited children under five years of age (n=5 versus n=1).

Thirty-nine studies were included in the review (from 989 potential studies) and meta-analysis revealed that with lifestyle interventions BMI SDS changed significantly by -0.16 (95% CI -0.24, -0.07, p<0.01) at 12-months. In practical terms, this treatment effect could mean that an individual child either maintained or lost weight while they grew. For example, a 9-year old girl weighing 60 kg and measuring 140 cm would have a BMI of 30.6 kg/m^2,

a BMI SDS of 3.48 and her BMI would plot above the 99.9th centile. If after 12-months of treatment she had maintained her weight but she had grown by 0.5 cm, she would then aged 10, have a BMI of 30.4 kg/m^2, a BMI SDS of 3.24 and her BMI would still plot above the 99.9th centile. The treatment effect in this case would be a reduction in BMI SDS of 0.24, which would be considered clinically successful. In this case however, the child is still classified as morbidly obese and would need on-going monitoring in line with a chronic care model of treatment.

It is likely that the child above would need follow-up until she reached puberty. For example, if this child was reviewed annually until aged 14 and at that point she weighed 63 kg, was 160 cm tall then she would have a BMI of 24.6 kg/m^2 and a BMI SDS of 1.60. Subsequently, her BMI would plot just under the 95th centile and she would likely have reduced co-morbidities. In turn, if she remained below this centile she would likely have a reduced risk of future adult illness (103).

The observed treatment effect in **Study 1** is slightly larger than the observed change of -0.14 (-0.17, -0.12) in the 2009 Cochrane review. Such differences may be accounted for by the use of random effects model in this review compared to a fixed effects model in the 2009 review. The difference may also be due to the larger sample size in this review or due to an improvement in the content and delivery of family-based obesity treatment.

Unlike the Cochrane review it was not possible to separate studies according to age group as the majority of studies recruited both children and adolescents to the same intervention. It is likely that an intervention that works effectively for children under 10 years would not be guaranteed to have the same effect in older children or adolescents. Younger children have a shorter history of unhealthy behavioural habits and have a greater height potential. Therefore younger children require weight stabilisation or moderate weight loss to achieve a reduction in BMI SDS. Post-pubertal children and adolescents however, will often require greater weight losses in order to achieve a reduction in BMI SDS. Such weight losses may be more

difficult to attain if behaviour and habits are more engrained. In addition, an expected difference in treatment effect could be due to age-related growth and development.

Firstly, the rapid growth of children experienced during puberty results in a developmentally appropriate increase in weight and insulin resistance and both of these factors can confound the affect of treatments (104). Secondly, adolescents have greater exposure to additional drivers of obesity including: more fragile self-esteem (105); are more strongly influenced by their social network (106); are more likely to engage in risky behaviour in an effort to assert developing autonomy (107) and experience the increased effect of social disadvantage (108).

As such, the age and maturity of the child have ramifications for the type of intervention delivered. In order to make intervention comparisons clearer, future studies should describe how maturity levels and learning styles were addressed during the intervention and sub-groups according to age should report results.

With regard to the socioeconomic (SE) background of participants in obesity trials, many interventions recruited motivated families from middle to high SE backgrounds. Resource limitations also affect whether migrant children are recruited to obesity interventions. An investigation in New Zealand compared the change in BMI in children whose families were successful in a migration lottery programme compared to those who were unsuccessful. After 12-months 3-5 year old children who had emigrated from Tonga to New Zealand had higher levels of obesity and data observed an influence of dietary change on the level of obesity (109). As well as the higher levels of childhood obesity observed in migrant families, obesity levels appear to be higher in European populations that are socially disadvantaged (6, 10). It is essential that such groups have equal access to treatment.

In addition future studies should aim to be consistent in the definition used to describe overweight and obesity. Cut-offs used to define obesity by the

International obesity task force (3) and the World Health Organisation have become more consistent since the 2009 review however, differences still exist even when cut-offs are used. For example the 95th BMI centile cut-off is used to define obesity in US studies whereas in many European studies, the 98th centile is used. These differences are important when exploring the effectiveness of interventions, as it is 'easier' to reduce the BMI SDS in individuals who are less obese compared to those with more severe levels of obesity. Controversy exists regarding the use of cut-offs to define obesity in children and reviews on the topic recommend that percentile-based cut-offs relative to national reference data be used in clinical groups (110, 111) whereas cut-offs from IOTF would be more appropriate for epidemiological studies. The extended IOTF cut-offs (112) may be a useful addition to practice and it might be helpful if future studies of obesity interventions define participants using both national and international cut-offs.

Similarly, testing an obesity intervention in a group of children, which includes those who are overweight and obese, creates additional difficulties when estimating the treatment effect. In many cases, the more obese a child is, the more difficult they may be to treat. Co-morbid conditions and the body's efforts to 'defend' the obese state can increase the treatment resistance of a child who is obese compared to an overweight counterpart. Firstly, co-morbidities including breathlessness, sleep apnoea, musculoskeletal pain and increased feelings of hunger can limit a child's ability to achieve the behavioural change required for weight maintenance or weight loss. Secondly, the physiological set-point theory posits that the amount fat tissue in the body is regulated by signals sent from adipose tissue to the brain (113, 114). These signals are thought to trigger changes in energy intake and/or energy expenditure in order to bring the levels of adipose tissue in line with the set point. If interventions include a group of widely heterogeneous participants and also do not clearly report the treatment effects according to level of obesity, the reader might incorrectly assume that a certain treatment would work for any given child. If future studies recruit children who are overweight and obese to intervention

studies, it would helpful if baseline adjustments are made for statistical analysis and that results describing the treatment effect are reported according to severity of obesity. This would aid the reader in drawing conclusions regarding the benefit of treatment for those most severely affected and will allow important comparisons of interventions in high-risk groups who might be considered for surgical plus lifestyle treatment rather than lifestyle-based treatment alone.

Nearly a third of the studies included in the review compared experimental treatment to a no-treatment control group. When exploring the effects of interventions on obesity prevention or in studies recruiting children who are overweight or mildly obese the use of a no-treatment control group may be advisable. However, the use of a no-treatment control group is controversial in the area of childhood obesity treatment given that timely treatment is recommended. Randomising children to receive no-treatment is considered unethical by some clinical researchers and instead studies should employ a usual-care group as a control. Inclusion of a usual-care group may however increase the difficulty of conducting clinical trials of interventions but this is perhaps a necessary challenge if clinical guidelines are to be followed and treatment not be withheld from patients. For example, withholding treatment from adolescents who are morbidly obese by randomising them to a no-treatment control group could indeed cause harm, as obesity is likely to increase and thus become more difficult to treat.

Compared to the 2009 review, more studies reported the use of power calculations but there were similar observations regarding attrition. Dropouts from the interventions reviewed ranged from 2%-60% and like the 2009 review less than 50% of studies performed an intention-to-treat analysis. Few studies reported on methods used to minimise dropouts and for those studies with high retention such detail would be helpful. In particular the use of technology should be described as tools such as short messaging services (SMS texting) and phone calls may help to reduce attrition.

Two-thirds of the studies reviewed detailed the behaviour change theory underpinning the intervention used and this is an improvement on the 2009 review. To allow replication of studies it would be helpful if studies detailed each intervention component and mapped each one to behaviour change strategies and techniques. The content of each intervention was not fully described in many studies and future studies should describe in detail which behavioural goals are promoted (e.g. to increase physical activity in general or to increase moderate-vigorous physical activity to at least 60 minutes per day). Overall, interventions address nutrition, physical activity and behaviour change. Few studies highlighted improving sleep as a treatment aim and more often than not, healthy hydration was not addressed. Instead interventions reported on reducing consumption of sugar-sweetened drinks. In addition, many interventions aimed to change behaviour however the use of age-appropriate valid and reliable outcome measures was inconsistent. Recent work by Bryant *et al.* (115) proposed the use of a framework of outcome measures for use in the evaluation of obesity interventions. The Childhood obesity treatment evaluation Outcomes Review (116) details a number of appropriate measures for use in domains such as physiology, mental health, quality of life and physical fitness and future studies should attempt where possible to follow this framework.

Building on the 2009 review, studies included in this review did use a greater variety of secondary outcome measures in addition to BMI such a quality of life measures, time spent in physical activity, physiological measures and measures of self-esteem. Few studies included measures of cost and future studies should aim to capture costs in order to allow comparison between interventions and establish the cost-benefit of one intervention over another. Inclusion of cost data is vital as healthcare systems will likely need to plan a variety of interventions for delivery to families depending on geographical location, severity of obesity and the presence of co-morbid conditions. Adverse events were included as secondary outcomes in six studies and these studies did not observe any such events. The inclusion of adverse events in studies is important as

weight loss in growing children can impair linear growth (117, 118), can delay puberty (119) and can reduce bone health (120). In addition, concerns exist regarding the development of disordered eating (121), negative psychological effects (122) and stigmatisation (123, 124) as a result of weight management in children. Accurate screening for adverse events is recommended for future trials and a recent position paper by the European Childhood Obesity Group on the assessment of eating disorders may assist clinicians and researchers to screen more accurately for eating disorders in study participants and thus adjust interventions and statistical analyses accordingly (Appendix).

In the 2009 Cochrane review, BMI SDS reductions of -0.06 (-0.12, -0.01) and -0.14 (-0.17, -0.12) were observed at 6-months in children (n=301) and adolescents (n=291) respectively. Significant changes in BMI SDS at 6-months of between -0.03 and -0.59 were observed in this review. Treatment outcomes varied according to the age, gender and baseline obesity level of participants. We observed a 12-month pooled difference of -0.16 (-0.24, -0.07) for 1342 participants, which is slightly larger than the observed change of -0.14 (-0.17, -0.12) for adolescents (n=231) in the 2009 review. Such differences may be accounted for by the use of random effects model in this review compared to a fixed effects model in the 2009 review. The difference may also be due to the larger sample size in this review or due to an improvement in the content and delivery of family-based obesity treatment. Results of this meta-analysis revealed that there was a high level of statistical heterogeneity observed (I^2 value of 81%) and this was similar to that observed in the 2009 review (I^2 value of 93%).

A reduction of BMI SDS of at least 0.1 is needed for associated improvements in health and ideally interventions should be achieving a reduction of at least 0.25 so that cardiometabolic health is improved. Achieving such changes in practice is extremely challenging and depends on how an intervention is tailored for the families being treated, how engaged families are with treatment and how accessible the intervention is for those

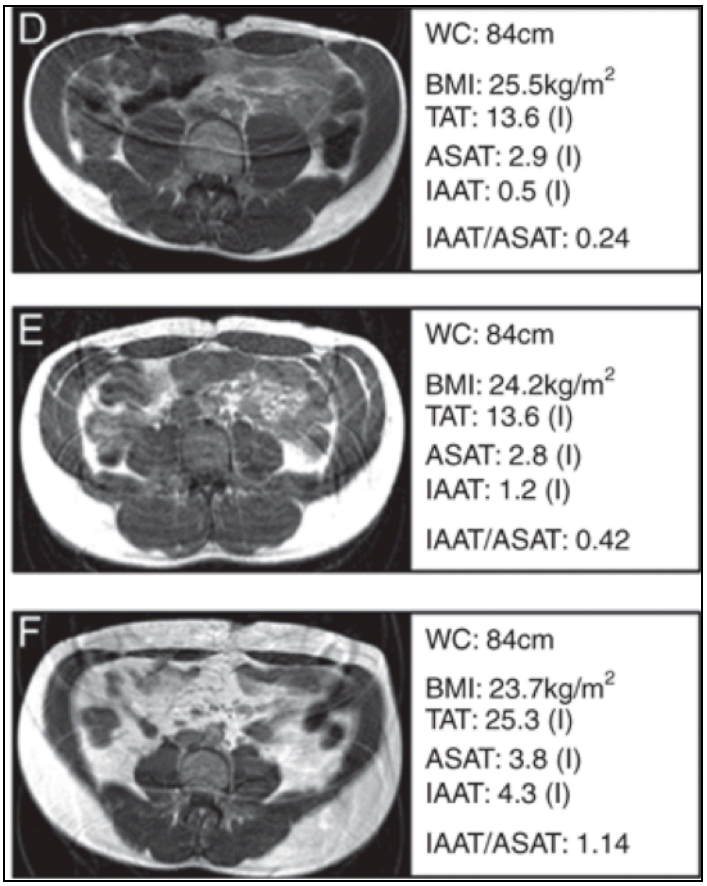
who need it most. Future studies should explore the longer-term effects of family-based interventions on obesity levels in the child and also should explore the effect of intervention on other parameters of health in parents and other family members.

Finally, a consensus is needed around whether BMI or its derivatives are the most appropriate primary outcome measures to use for diagnosing paediatric obesity or indeed for the evaluation of treatment. BMI is a simple measure to calculate in practice and is very useful in large population studies. However BMI relies solely on body weight and height disregarding the body composition of the individual (125). In addition, there are racial, ethnic, gender and age differences in how and where the human body stores adipose tissue (126-128). In adults with the same waist circumference higher stores of visceral fat are observed with increasing age (129) as depicted in figure 2.3. Similarly, children of Hispanic ethnicity store more fat in visceral compartments compared to African-American children who have greater subcutaneous fat tissue stores (and thus a lower risk of cardiometabolic disease). A recent meta-analysis observed that BMI had a high specificity but low sensitivity to detect excess adipose tissue in children (130). The report concluded that BMI failed to identify 25% of children with excess fat as determined by reference methods for measuring body composition. Such evidence highlights the importance of including a number of health-related outcome measures when estimating the impact of obesity on the health of the child and when evaluating interventions aimed to attenuate this impact.

2.7 Part A: Conclusion

This review and meta-analysis indicates that family-based lifestyle interventions are a promising form of treatment for paediatric obesity. Lifestyle treatments addressing nutrition, physical activity and behaviour change can significantly reduce obesity at 12-months.

Figure 2.3 MRI images of visceral fat deposits from Kuk et al.[129]



Anthropometric variation in abdominal adiposity. Umbilical MRI images obtained from three different male subjects with the same waist circumference (84 cm.) but with different volumes (litres) of total adipose tissue (TAT), subcutaneous abdominal adipose tissue (ASAT) and intra-abdominal adipose tissue (IAAT).

2.8 Part B mHealth interventions: Abstract

Background A growing body of research has employed the Internet and mobile phones in the treatment of obesity. Few studies have focused on the use of mobile-health tools in child and adolescent interventions.

Objectives The present study aimed to review and systematically evaluate the efficacy and methodological quality of mobile-health obesity interventions for children and adolescents.

Methods Electronic databases were searched and articles that provided descriptions of m-Health interventions designed to treat overweight and obesity in children and adolescents were included. A meta-analysis of treatment effects on BMI SDS at 12-months was conducted using a random effects models.

Results: From 9,103 titles, six were eligible for inclusion in the review. Studies used a range of mHealth tools including: interactive voice messaging systems; tailored text messaging; website interventions and telephone coaching. Four studies were combined in the meta-analysis and an overall statistically insignificant change in BMI SDS of -0.03 (-0.13, 0.06) at 12-months was observed.

Conclusions: Results of this study indicate that mHealth interventions may be useful as adjuncts to treatment. Further study is required to investigate the potential of mHealth tools in managing obesity in children and adolescents.

2.9 Part B mHealth interventions: Background

Traditionally, healthcare interventions have involved face-to-face contact between clinicians and patients, however paradigms for health assessment and treatment have evolved to include specialist referral systems, patient call centres, patient consultation via video conferencing, electronic patient portals and remote monitoring via biomedical sensors. In addition, therapeutic strategies such as online computer-based interventions, mobile phone short message services (SMS/texting), remote rehabilitation and gaming consoles have been used as tools to deliver treatment. Such approaches come under the umbrella term of telemedicine, broadly described as medical information exchanged from one site to another via electronic communications to improve patients' health status.

Though telemedical approaches are not without challenges, evidence is emerging that telemedical strategies can augment the patient-carer interaction and support delivery of healthcare (131). With the advent of mobile telephony, patient data can be collected, analysed to assist with diagnosis and used to direct therapeutic strategies. Evidence regarding the use of telemedical approaches exists in areas such as: clinical education (132); dissemination of health information (133, 134); healthcare data collection (135); for the provision of remote healthcare services (136-138); for tracking of symptoms (139); for behavioural interventions via SMS (140, 141); and to improve medication and therapy compliance (131, 142). Although economic benefits have been reported where mobile communication is used for the provision of healthcare in remote geographical regions (143), establishing and maintaining the necessary infrastructure and protecting private patient data post significant challenges.

The emergence of smartphones as computing handsets offering voice service in tandem with native software applications and the ability to run Internet-based software has heralded the term ‘mobile Internet’ (144, 145). Mobile cellular phones, smartphones, tablet and notebook devices are of

particular interest in healthcare as their portability releases the user from being attached to a particular location (e.g. a desktop computer). Globally, 968 million mobile phones were sold in 2013 with smartphones making up 54% (146) and the number of all mobile devices sold in 2014 (tablets and mobile phones) is projected as 2.2 billion (147). The ubiquitous nature of these devices is particularly relevant to the health sector where their potential use for the delivery of therapeutic support and mobile health (mHealth) interventions is promising.

Paediatric obesity and mHealth

Globally paediatric and adolescent obesity has reached epidemic levels with 170 million children estimated to be overweight and obese (148). Obesity in childhood is associated with signs of early cardiovascular disease, impaired quality of life, metabolic dysfunction, musculoskeletal impairment and social isolation (21, 149-152). Additionally, obesity in adulthood is associated with non-communicable diseases (cardiovascular disease, Type 2 diabetes, and certain cancers), which lead to long-term morbidity and premature mortality (153). Worryingly, obesity incurs not only health costs but the financial costs are staggering with an annual Irish spend estimated between 0.6 and 9.1% of total healthcare costs (34).

Recently, a Cochrane systematic review concluded that interactive computer-based interventions were effective for weight loss or weight maintenance in people who were overweight or obese as compared to no intervention or minimal intervention (43). The meta-analysis of 2,537 participants described six-month weight losses of 1.5kg (95% CI 0.9-2.1), which were superior to minimal interventions but inferior to face-to-face interventions. With the advent of web-enabled mobile devices, it is not currently known whether such portability will enhance the effect of computer-based telemedical interventions. MHealth interventions have been used as therapeutic weight management strategies in adults (46-48, 50, 154), but data regarding the use of mHealth interventions in paediatrics are sparse. Part A of this chapter described the face-to-face interventions

used in family-based treatment and highlighted the challenges of delivering obesity treatments. Limited staffing and patient access to specialty centres, plus, the chronic nature of clinical obesity impact on the manner by which health services can deliver treatments. It is possible that lifestyle interventions could be augmented and their effectiveness optimised by using modern technology to enhance communication between the patient and the clinical team.

2.10 Part B mHealth interventions: Aim

The aim of this study is to review the current available evidence regarding the effects of mHealth obesity interventions in the treatment of paediatric and adolescent obesity.

2.11 Part B mHealth interventions: Method

This review was conducted in line with the PRISMA guideline (59) and recommendations of the Cochrane Collaboration.

2.11.1 Study design

Studies were eligible for inclusion if they met the following criteria:

- Study described a randomised controlled clinical trial of an intervention designed to treat obesity;
- Study was written in English;
- Study recruited community-dwelling children and adolescents (0-17 years) who were overweight or obese (described using standard objective methods, BMI cut-offs or percent overweight);
- Intervention addressed lifestyle change (nutrition, physical activity and behaviour change);
- Intervention was delivered using an mHealth approach (defined as any intervention that used a mobile technology to deliver treatment. Mobile technologies included mobile phone voice-calls, short messaging services/SMS, texting personal digital assistants, laptops,

tablets and smartphones);

- Study specified body mass index (BMI), BMI standardised deviation score (BMI SDS) or BMI percentile as a primary outcome measure;
- Follow up data was reported at least three-months post baseline measurement.

2.11.2 Information sources

An electronic search of the following databases was conducted: Medline, CINAHL, Academic Search Complete, Business Source Complete, EconLit, MEDLINE, PsycARTICLES, PsycINFO, SPORTDiscus, and UK & Ireland Reference Centre to retrieve English language articles published in peer-reviewed journals from January 1, 1970, through December 4 2013.

2.11.3 Outcome measures

The primary outcome of interest was standardized measurement of overweight or obesity as defined by the body mass index (SDS / percentile). Secondary outcomes included body composition measures such as waist circumference and body fat percentage; measures of health variables such as blood profiles and measures of intervention adherence were also noted.

2.11.4 Search

The search terms used were:

- Child OR adolescen* AND
- Obesity OR obes* OR behav* AND
- Treat* OR interven* AND
- Phone OR Internet OR online OR handheld OR smart*.

Filter limiters were used to identify clinical trials conducted in humans only and published in English.

2.11.5 Study selection

Titles identified during the search procedure were screened for relevance, and those titles that did not meet the eligibility criteria were excluded. Relevant abstracts were imported into Endnote bibliographic software (Endnote 7.0, Thomson-Reuters, New York) and abstracts were screened using a data collection tool (Appendix I).

2.11.6 Data collection

The full-text papers of eligible abstracts were reviewed and data related to study participants, study design, control group, attrition, intervention components, underlying theory, outcomes, and treatment effect were collated. In addition, data that may have increased the risk of bias were noted (e.g. randomisation and allocation methods used, validity of outcome measures, incomplete data, selective outcome reporting, group differences at baseline, protection against contamination and publication bias).

2.11.7 Data analysis

Data from eligible studies was entered into RevMan software (version 5.2.1) and the mean changes and standard deviations of BMI SDS were pooled using a random effects model. If the data in a study was reported as baseline mean and 95% confidence intervals, the mean change and standard deviations were calculated using methods recommended by the Cochrane Collaboration (60). A forest plot of the weighted pooled effects and the associated statistical heterogeneity was calculated using RevMan.

2.12 Part B mHealth interventions: Results

Searching identified 9,103 potential studies. After screening the titles for eligibility, 1,588 studies were included for further assessment and from these 35 full-papers were reviewed. Six studies met the criteria for inclusion in the review. Figure 2.4 details the reasons that studies were excluded from the review using a PRISMA flow diagram.

2.12.1 Participants of included studies

Table 2.2 details the characteristics of each of the six included studies. Participants aged 8-16 years were recruited to the included studies and most studies (n=4) detailed the definition of obesity used for eligibility.

2.12.2 Study design of included studies

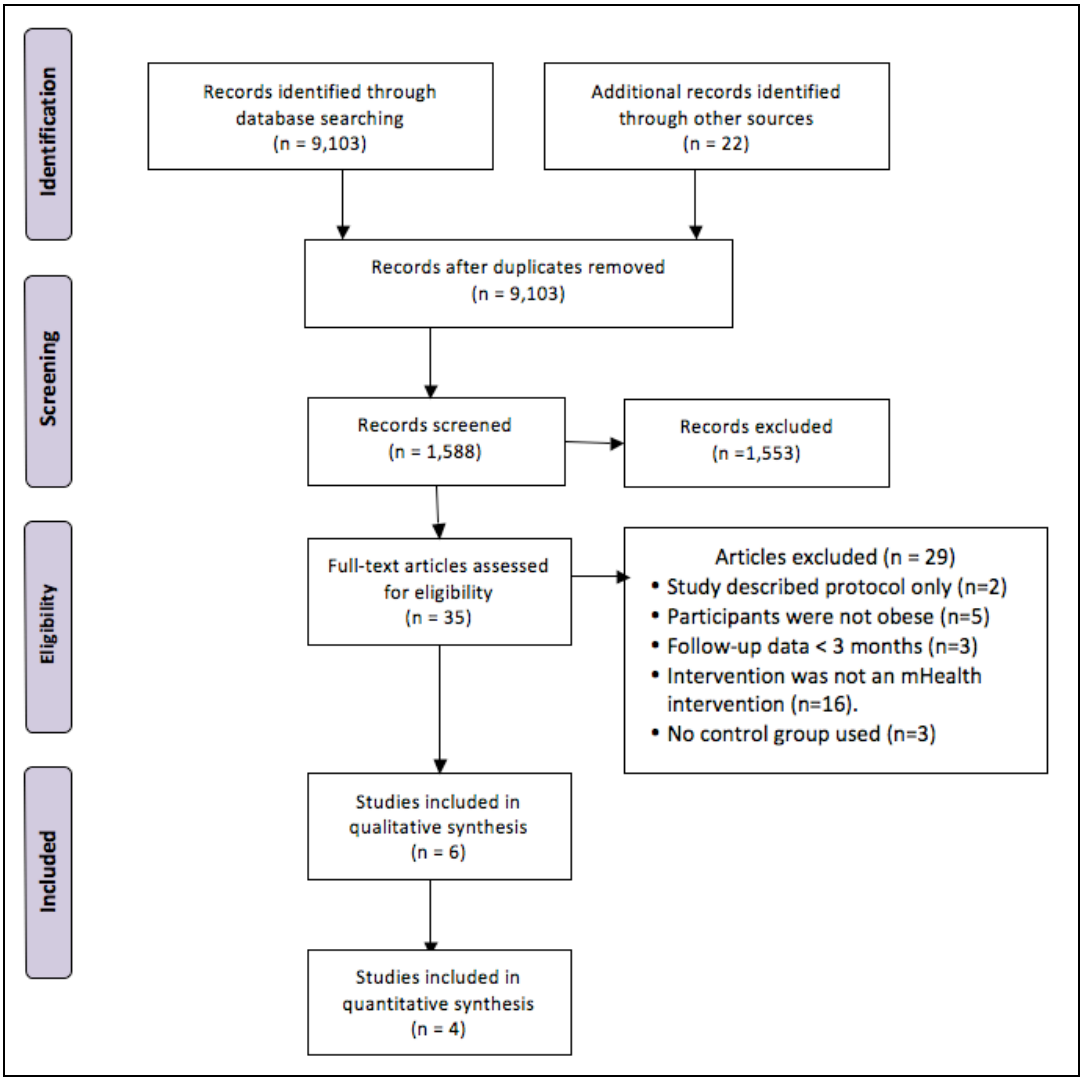
All studies included in the review were randomised and controlled with sample sizes ranging from 20-220 participants. Most of the studies reported a power calculation (n=4) and stated the behavioural change theory on which the intervention was based (n=5).

MHealth interventions were delivered following or in addition to a face-to-face treatment in five of the six included studies. In a study by De Niet *et al.* (155), 144 participants completed three months of a family-based lifestyle intervention and were then randomised to either receive a mobile phone plus tailored text messaging or usual-care follow up for nine months. Similarly, in a group of children who had completed an inpatient obesity treatment, Deforche *et al.* (156) randomised participants to receive either three-months of contact by phone or no contact. In Nguyen et al (157, 158), 12- and 24-month outcomes were compared in 151 adolescents randomised to receive additional therapeutic phone coaching versus a control group who attended 3-monthly booster group sessions. In Estabrooks *et al.* (159), 220 participants were randomised to receive either a family workbook, a workbook plus group sessions with a dietitian or workbook, dietetic sessions plus interactive voice response sessions using an automated system. One study compared an mHealth intervention with a control intervention in parallel study arms. Patrick *et al.* (160), randomised 101 adolescents to receive treatment via a website, via usual clinic care, via a website plus group sessions or via a website plus text messages.

Text messaging and phone-calls used in the above interventions aimed to reinforce positive behaviour change and promoted increased physical activity, consumption of fruit and vegetables, goal setting and self-

monitoring. Both DeNiet *et al.* (155) and Patrick *et al.* (160), provided study participants with a cell-phone for the study duration while the other studies required participants to use their personal phones.

Figure 2.4 PRISMA flow diagram of studies included in the review of mHealth interventions for paediatric obesity



2.12.3 Outcome measures of included studies

The six included studies used a range of outcome measures for monitoring of anthropometry, physical activity level, sedentary time, wellbeing, metabolic health and quality of life.

Five studies measured change in BMI whereas Deforche *et al.* measured the amount of weight regain during the mHealth intervention. Half of the studies reported monitoring adverse events and no such events were observed throughout the study periods.

Attrition varied across studies and in the case of Deforche *et al.* no details were given regarding dropouts. In four studies (155, 157, 159, 160) drop out numbers were lower in the mHealth intervention compared to controls however Nguyen *et al.*, observed greater retention in the usual care group compared to the mHealth group over 24 months of follow up (161).

2.12.4 Treatment effect of included studies

2.12.4.1 Treatment effect at 6-months

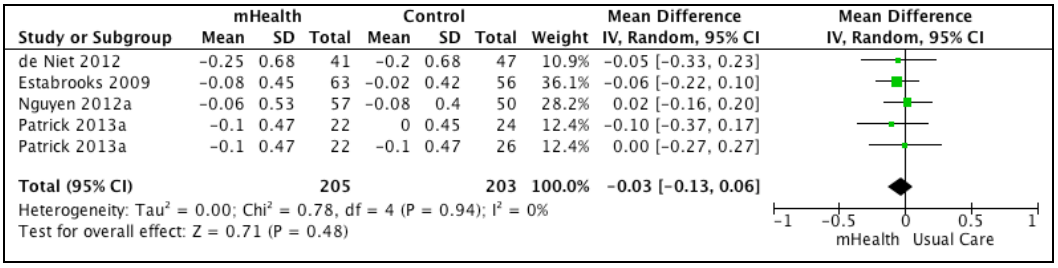
Treatment effects of mHealth intervention ranged from a 6-month increase in BMI SDS of 0.01 in deNiet *et al*, to a statistically insignificant reduction of 0.01 in Patrick *et al*, to a statistically significant reduction of 0.04 in Estabrooks *et al.* Deforche *et al.* reported that weight regain was significantly less ($p<0.05$) in a group receiving telephone contact compared to the control group receiving no contact. When the 6-months results were pooled, the overall effect size was a reduction in BMI SDS of 0.02, which was statistically insignificant.

2.12.4.2 Meta-analysis of treatment effect at 12-months

Four studies reported 12-month BMI SDS follow-up data and were included in the meta-analysis. Patrick *et al.*, observed no significant treatment effect of a web-based intervention on BMI but did observe that website plus group sessions plus telephone follow-up reduced sedentary behaviours. Nguyen *et al.* found no difference in 12-month outcomes between participants receiving additional contact by phone versus those in the usual no-phone group. Similarly, de Niet found no difference between those receiving text messages and those receiving usual care. However, the authors did observe that weight loss was positively correlated to use of the texting system in the first three months of treatment.

The pooled mHealth treatment effect was a reduction in BMI SDS of 0.03 however this was not statistically significant. Figure 2.5 details the meta-analysis results and forest plot.

Figure 2.5 Pooled treatment effect of mHealth intervention on BMI at 12-months



2.13 Part B mHealth interventions: Discussion

This study reviewed the current evidence regarding the use of mHealth tools in paediatric obesity treatment. The majority of studies tested an mHealth intervention against a control condition during the maintenance phase of obesity treatment. In these cases the mHealth tool was used to augment a traditional face-to-face treatment. In Patrick *et al.*, an mHealth intervention was compared to a usual care control. No differences in BMI reductions were seen across the study arms however a significant change in sedentary time was observed in the group using the intervention website compared to those receiving usual care.

Statistically significant reductions in BMI were observed by Deforche et al using follow-up calls with teenage patients during. Similarly, Estabrooks used an automated voice response system for parents of children who were obese and observed significant reductions in BMI. Given the ubiquity of mobile technologies mHealth interventions could be promising for the delivery of obesity interventions however, the results of this review indicate that mHealth interventions do not significantly reduce BMI in children and adolescents. The remaining discussion will highlight a number of factors, which should be considered when developing, and testing mHealth

interventions in the field of obesity. These factors are drawn from studies identified during the search procedure for this review.

2.13.1 mHealth interventions as stand-alone treatments or to augment usual care

Attempting to augment the patient-clinician relationship with technologies such as texting, email and voice response systems, is appealing however a number of factors which influence the expectations of those involved need to be considered. Online patient forums or patient social networking apps run the potential risk of promoting inaccurate information, which traditionally would be managed on a day to day basis by the clinician. Appropriate moderation of such online services is recommended for future studies. In addition, the use of a health-certificate would be useful so that the public can decipher between web-based sources of health information that are evidence-based rather than those that are editorial opinion. Secondly, the bond between clinician and patient is based on trust and empathy and in interventions such as obesity management agreed goal setting, honest reflection and problem solving are key characteristics, which are employed. It is not clear whether remote treatment interventions can beneficially replace or augment this. There are reports of stigmatising and discriminating attitudes by healthcare professionals towards children who are obese (123, 124, 162). In such cases, effective remote treatment with appropriately trained professionals may be preferable to treatment delivered on an ad-hoc basis by health professionals who fail to understand the complexity of obesity or fail to address potential treatment barriers such as prejudice and stigma.

The development of telemedicine has brought with it a number of technology-specific challenges. Recipients of mHealth interventions may have conflicting expectations of how a service will function and it is important that the user is aware of how immediate responses from the clinician will be, particularly in cases where SMS or push notifications are used (163).

2.13.2 Regulation of mHealth interventions

Healthcare providers attempting to provide remote treatment options should be fully aware of the regulatory environment to which they must conform (164). Development of smartphone applications as treatment tools should follow best practice guidelines regarding human-computer interaction and integration of monitoring devices or bio-sensors with smartphones will likely need to align to EU and FDA medical and electrical device regulations (165). Similarly, it is important to consider whether the hardware (e.g. mobile phone or remote sensor), the components (e.g. electronic component or software) and the accessories (e.g. mobile application) used in an mhealth tool are developed in accordance with harmonised global standards and requirements of the International Organization for Standardization (e.g ISO13485 and IEC 62304).

Design and development of technology-based interventions will need to be accessible so that individuals with disabilities are not precluded from using such treatments. Optimal functioning and reliability of the software and device are essential for usability (166) and future studies should report on the beta testing and usability testing of the intervention. Technical issues such as optimizing battery life and provision of multi-tasking capabilities are of particular concern for mHealth interventions using smartphones and tablets. For example, if a smartphone application is tested to monitor physical activity in a group of teenagers, use of the application (and therefore treatment effect) might be influenced by the following factors: whether a data plan is provided by the study; the type of phone the participant uses and whether this is optimised for the new application; and whether the application is constantly running and therefore using battery power. Standardising the type of device utilised in a study might assist in controlling for such differences.

2.13.3 Data protection

Accurate collection of patient-related data and subsequent mHealth

intervention delivery hinges on the transference of private and confidential patient-related data. Such data is at risk if an mHealth device is lost or stolen and as such password protection and data encryption can assist with securing data. Similarly, patient-sensitive data should be securely managed so that personal details are not distributed to third party companies (167, 168). In the area of mHealth it is vital that users and clinicians are informed regarding the manner in which data is stored and shared. Similarly, 'Big Data' processing methods will need to be optimised to allow integration of the estimated petabytes of data (169) collected from mHealth applications used within the wider health system.

2.13.4 Adverse events

A further consideration regarding mHealth intervention is the recording and reporting of adverse events. The studies included in this review reported no adverse events and the only measure used to monitor adverse outcomes was an eating disorder questionnaire. Future research will need to include methods of recording not only adverse events related to the intervention but also related to the use the mobile device itself. For example, controversy exists regarding the physiological impact of exposure to the electromagnetic field (EMF) and radiofrequency field (RF) emitted from mobile devices. The WHO International EMF Project was established in 1996 to assess the scientific evidence regarding the health effects of EMF (0 to 300 GHz). Issues of concern include the possible associated risk of brain tumours, headaches, sleep disturbances, and cell damage (170-172). Recommendations have concluded that no adverse effects have been found from exposure to the RF signals produced by mobile phones but that more research is required in children where studies of adverse health effects have been inconclusive (173-177). It is vital that future research involving the delivery of healthcare via remote devices should aim to document adverse symptoms. Adverse symptoms reported to date include sleep disorders, headaches, nervousness or distress, fatigue and concentration difficulties. These symptoms are otherwise known as electromagnetic hypersensitivity or idiopathic

environmental intolerance attributed to electromagnetic fields (178).

In addition,

2.13.5 Ethical considerations

The use of mHealth tools and interventions poses some unique ethical challenges. Growth in the electronics industry has had an environmental impact as disposal and recycling of old electronics and plastic parts creates a large ecological footprint. Mobile devices contain heavy metals such as lead and mercury, which need to be disposed of safely in order to avoid contamination of our water supply. The United Nations Environment Programme estimates that a majority of the annual 50 million tonnes of electrical waste generated in the West is disposed of in developing nations (often in countries where facilities for safe disposal do not exist). If the healthcare sector is to promote mHealth interventions for one group of patients, it will be essential to ensure that unanticipated health impacts are not created for another group of individuals.

Similarly, growth within the mobile device industry appears to have a political impact. Tantalum used in the production of electronic capacitors is derived from the mineral Columbo-Tantalite (Coltan). Increased mining for Coltan has been cited as an influential factor in illicit trade, conflict and environmental devastation (179, 180). Any serious attempts to integrate technology and mHealth into global healthcare should be coupled with strategies to optimize environmental sustainability and Fair trade.

2.13.6 The future

Imagining what the future of mHealth will look like is not easy as technologies continue to advance at an exponential rate. It is clear though that given the scalability offered by the mobile platform, applications deemed to be useful by the end user could yield beneficial outcomes in terms of public health. Many of the substantial advances in knowledge sharing and technology-based solutions have to date, been driven by the end

user. Taking the case of computerized retail banking as an example, von Hippel and Oliveira (181) describe the evolvement of "lead user innovation" whereby a large portion of both computerized commercial and retail banking was first developed and implemented by service users rather than the banking industry. The possibility of the end-user developing and testing innovative and effective methods of collecting, delivering and sharing secured health-related information is promising. As such, there are few reasons to assume that healthcare would be different. The challenge will be to harness the "cognitive surplus"(182) of today's tech-savvy global population so that innovation might drive effective solutions to public health challenges. Online social networks continue to grow as populations attempt to connect with one another and engaging the end-user in the process of designing evidence-based health strategies might enhance treatment or prevention outcomes. It may be possible to harness such activity to facilitate effective peer support and motivation via the online social network (183). Technology will not replace in-person healthcare treatment per se but it may improve the effectiveness of large-scale interventions and alter the face of healthcare as we currently recognize it (184). Regardless, it is clear that effective interventions should be evidence-based and rigorously tested in order to estimate both clinical and cost effectiveness.

2.14 Part B mHealth interventions: Conclusion

MHealth interventions are promising methods of augmenting traditional treatment of paediatric obesity. Based on current evidence, it is not recommended that traditional forms of treatment for child and adolescent obesity be replaced by mHealth interventions.

2.15 Acknowledgements

Sincere thanks to Bernadette Colley, the hospital librarian assistance with retrieval of full-text papers. The candidate is responsible for the study design, data collection, data analysis and writing of the paper.

Table 2.1 Characteristics of studies included in the systematic review of face-to-face lifestyle interventions for childhood obesity

Study	*Arauz Boudreu et al.. 2013*	*Barkin et al.. 2011*	*Bathrellou et al.. 2011*
Participants	41 OW/OB (>85th BMI Centile) Latino children (9-12 yers) recruited from primary care centre.	106 children (8-11 yrs) (BMI>85th) & parent. Recruited from clinic & community	47 OW/OB children (9 yrs)recruited from hospital. Child only (n=23), child+ parent (n=24)
Study design	6-month RCT of treatment versus waiting-list conttrol. PC present.	6-month RCT No randomisation detail. No PC.	RCT comparing parental involvement. 6- and 18-months. 23 in child+parent, 19 in child only. No randomisation detail, no PC.
Intervention	Treatment was made up of group education (activity classes, nutrition behaviour change) + family coaching. Delivered in a community health centre 90 mins x 5 weeks with 6th week 1 month later + coaching monthly throughout 6 months.	6 sessions: 1st session at clinic: motivational interviewing, goal setting, & group education on increasing physical activity. 5 group activity sessions at YMCA Control is 2 standard clinic visits & group discussion on healthy lifestyle.	3-month weekly MDT programme delivered 1:1 with dietitian + 6 monthly boosters with our without parent.
Underlying theory	Goal setting and Latino diabetes programme.	Transtheoretical model	Cognitive behavioural therapy
Outcomes	BMI, body fat, laboratory measures, quality of life, physical activity. No AE reported.	Child & parent BMI. No AE reported.	% Overweight. No AE reported.
Attrition	36%	32% for treatment.	11% refusal.

Power calculation (PC). Adverse Events (AE).

Study	Berkowitz et al.. 2011	Bocca et al.. 2012	Boutelle et al.. 2011
Participants	120 obese adolescents (15 yrs)	75 OW/OB children (3-5 yrs) referred to clinic.	80 OW/OB children (BMI>85th) (8-12 yrs) recruited from community & clinic.
Study design	12-month RCT. No randomisation detail or PC.	RCT comparing 4-months of MDT (N=40) intervention to usual clinic care (N=35). Computerised allocation. No PC.	RCT to compare 5-months of child+parent (PCh) or parent only (PO) treatment. Computerised allocation. No PC.
Intervention	4 months of lifestyle modification + conventional diet or meal replacements + 8 months of either diet. Lifestyle: weekly group meetings- increase activity to >30 min/day, reduce sedentary time. Parents met as a group separate to kids. Conventional diet of 1,300-1,500 kcal/day or isocaloric diet of 3 free Slimfast shakes, 1 prepacked meal of choice and 5 servings of fruit + veg.	MDT: 6x30min dietary advice sessions (breakfast daily, abstain from soft drinks and 3 snacks/day) + 12x60min activity (motor skill, fun and habitual activity of 60 mins/day) sessions and 6x group behavioural therapy session (120mins). 30hrs in 16 weeks. UC: 3x30-60mins with paediatrician during 16 weeks (info on healthy eating + behaviour).	PCh: Traffic light diet, behavioural change skills, increase in activity, reduce sedentary time + games + quizzes. Delivered in 60-min groups parents separate to children for PC. For PO, parents seen in groups.
Underlying theory	Behavioural self-monitoring, stress management, stimulus control, social support, problem solving.	Goals setting, positive reinforcement	Behaviour change as per Epstein intervention.
Outcomes	BMI, %change BMI, depression & eating inventory, blood pressure and blood tests. No AE reported.	BMI, physical activity, body fat, waist/hip. No AE reported.	Parent and child BMI, BMI SDS, BMI Centile, physical activity and diet. No AE reported.
Attrition	9% refusal and 33% dropout	16% at 12 months. 20% MDT, 11% UC	6 month: 40% in PO, 30% in PC

Study	Boutelle et al.. 2013	Chen et al.. 2010	Collins et al.. 2011
Participants	50 OW/OB (BMI>85th<98th) children (8-12 yrs) community & clinic.	67 children (8-10yrs). All weights. No recruitment details.	165 OW children (5-10 yrs) with mean BMI SDS 2.8. No recruitment details
Study design	RCT of guided self help to waitling list control. Computerised allocation. No PC.	RCT of lifestyle programme (n=35) versus waiting list control group (n=32). Computer based allocation. PC given.	6-month RCT to compare 3 parallel group (diet+activity (n=70) programme against diet (n=63) or activity (n=73])only). Computer based allocation. PC given.
Intervention	12 visits over 5 months (every 2nd week for 20 mins) + self monitoring materials + participant manual including traffic light eating, stimulus control, increasing physical activity, decreasing sedentary time, motivation, teasing and relapse prevention.	Weekly 45 min group sessions for 8 weeks for children and 2x 2hr group sessions over 8 weeks for parents. Sessions aimed to increase self-efficacy through goal setting, achieve mastery and improve self-regulation of healthy lifestyle. Sessions targeted nutrition, physical activity (15min each week) and critical thinking. Payment for attending outcome measurement.	6-month programme. Weekly 2-hr session for 10 weeks with homework + monthly booster by telephone for 3 months.
Underlying theory	Not stated-includes self monitoring ad self regulation	Social cognitive theory.	Health belief model + competence motivation theory.
Outcomes	BMI, BMI SDS, BMI Centile and %OW physical activity and diet. No AE reported.	BMI, waist: hip, blood pressure, physical activity, food diary, food choices, self-efficacy. No AE reported.	Measured at 6, 12 and 24 months. BMI SDS. Waist, blood pressure, lipids, physical activity. No AE reported.
Attrition	12% for both groups.	15% @6/12	38% diet, 61% activity and 40% diet activity) @24/12.

Study	Coppins et al.. 2011	Croker et al.. 2012	DeBar et al.. 2011
Participants	65 OW (>91st BMI centile) children (6-14 yrs).	72 obese children (8-12 years) recruited from clinic.	208 Adolescent girls (12-17 yrs) >90th BMI centile recruited from HMO.
Study design	2 yr RCT comparing 12-months of active family-based intervention (n=35) against control (growth monitoring, n=30). No PC given.	RCT comparing family-based treatment to waiting list control. Computerised randomisation.PC given.	RCT of lifestyle treatment versus usual primary care visit. PC given.
Intervention	2 x Saturday group workshops (8h total) 1-2 weeks apart + 2 activity sessions of 1h/week over 12 months. Involved healthy eating, physical activity, reducing sedentary behaviour and well-being.	15 sessions of 90 mins over 6 months (10 weekly, 3 fortnightly and 2 monthly). Concurrent but separate parent and child groups.	16 x 90-min group sessions over 5 months. Weekly x 3 months (teens and parents) and biweekly for month 4 and 5. Self-monitoring, goal setting and review, change in dietary intake and behaviour, increase in physical activity (given yoga training, an exergame + pedometer), counselling and training for primary care team. If unable to attend were offered telephone session. Usual care got 1 visit with PCP + information on weight management.
Underlying theory		Learning theory including goal setting, positive reinforcement, stimulus control and self-monitoring.	Cognitive behavioural techniques. FRAMES for training of primary care team.
Outcomes	BMI SDS, waist, body fat, lifestyle, cost. No AE reported.	BMI SDS, weight, waist, fat mass index, blood pressure, psychosocial health. AE reported.	BMI SDS, dietary intake, physical activity, quality of life, self-esteem, psychosocial measures. AE not reported.
Attrition	23% (15% from intervention and 8% from control)	27% in treatment arm	6% at 6-months, 17% at 12-months.

Study	Diaz et al.. 2010	Duggins et al.. 2010	Ford et al.. 2010
Participants	76 children (9-17 yrs) >95th centile	83 OW children (>85th centile) (5-17 yrs) from clinical practice.	108 OB (95th centile) children (9-17 yrs) from clinic.
Study design	RCT comparing lifestyle programme to usual primary care clinic visit. Computerized randomisation. PC given.	12-month RCT. Computerised randomisation. PC given.	RCT. Computerised block randomistion. PC given.
Intervention	Lifestyle programme (child-only sessions x 12, weekly (2hr) + 1:1 sessions with the dietitian for 3 months and monthly thereafter + 6x parent session. + monthly primary care visit. Control group of monthly primary care visit with physical trained briefly on obesity management.	9 months of family-based nutrition evening nutrition classes x4 with (n=44) or without (n=39) 12-month family YMCA membership	Mandometer group attended training weekly x 6-weeks, then once every 2-weeks for 6 weeks & then once every 6th week. From week 12, patients received a phone call every 2nd week. Also met with dietitian & clinician 4 times over 12 months. Standard care every 3-months (goal setting and motivational interviewing).
Underlying theory	Health belief model.	Not stated	Reduced speed of eating increases satiety.
Outcomes	BMI, BMI SDS, body fat, blood pressure and laboratory tests. AE not reported.	Reduction in 2 BMI centile points, attendance at YMCA. AE not reported.	BMI SDS, body fat, laboratory tests, quality of life. AE reported=0.
Attrition	34% at 6-months 43% at 12 months	18% YMCA group, 30% control	17% in mandometer and 25% in control

Study	Garipağaoğlu et al.. 2009	Hystad et al.. 2013	Janicke et al.. 2008
Participants	80 children (6-14 yrs) self-referred to clinic.	99 OB (BMI SDS>2) children (7-12 yrs) from obesity clinic.	93 OW (>85th BMI centile) children (8-14 yrs) recruited from community.
Study design	12-month RCT. Computerised randomisation. PC given.	RCT comparing Therapist-led groups (TLG) and parent-led groups (PLG). Computerised randomisation. No PC.	RCT comparing family-based (FB) intervention with parent-only and waiting list control. PC given.
Intervention	3-month weight control programme based on Epstein's (included hypocaloric diet) (n=40) for 7 sessions (30-90 mins) every 2 weeks. Control group (n40) was treated individually x 30min sessions x 7 times in 3 months.	All children participated in group sessions every 2 weeks x 10 weeks (2hrs) + 5 monthly individual sessions with dietitian and physiotherapist. Therapist-led groups (TLG) and parent-led groups (PLG) aimed to establish health eating. TLG aimed to enhance parental competence for change and included goal setting, homework and role-play x 10 sessions (2hrs). SHG based on parents own knowledge and first 2 sessions facilitated by health professional. From month 6-24 groups met 5 times + 4x individual sessions.	4-month intervention with weekly 90-min sessions x 8 weeks and then biweekly for next 8 weeks. Modified traffic light diet with self – monitoring, & goal setting. Pedometers used to increase activity. FB sessions were for children and parents (seen separately). PO group focused on teaching parents how to set goals with their children.
Underlying theory	Family treatment as per Epstein.	Clinical guidelines.	Not stated.
Outcomes	BMI, BMI SDS, costs. AE not reported.	Body fat, BMI SDS, dietary intake. AE not reported.	BMI SDS, food frequency. AE not reported.
Attrition	5% (2.5% from treatment, 7.5% from control)	10% at 6/12,	4% at 10/12

Study	Kalarchian et al.. 2009	Kalavainen et al.. 2011	Lison et al.. 2012
Participants	192 OB (BMI >97th centile) children (8-12 yrs) recruited through universiy medical centre.	70 OB (weight for height 12—200%) from clinic.	110 OW (>85th BMI centile) children (6-16 yrs) from clinic.
Study design	RCT to compare family-based intrevention with usual care.PC given.	RCT comparing family-based intervention to usual care. No PC.	RCT comparing home- and group-based interventions with control. PC given.
Intervention	20 group sessions (60 mins) over 6-months. Parents and children met separately. 6 booster sessions (3x group + 3x phone call) between 6/12 & 12/12. Self-monitoring, goal setting, stimulus control and positive reinforcement aimed to increase activity, reduce sedentary behaviour and follow stoplight eating plan. Usual care group received 2 nutrition session based on the Stoplight eating plan.	6-months of intervention. Group treatment was 15 separate sessions for children and parents. Usual care was 2 individual sessions with a school nurse.	2x1hr education parent & child group sessions on nutrition (Mediterranean diet, reading food labels), reducing sedentary behaviour and weight management. Group participated in 5 60-min weekly exercise sessions for 6 months and home group were given a home exercise prescription. Controls had regular visits to clinic.
Underlying theory	Epstein programme	Not stated.	Not stated.
Outcomes	%OW. Body fat, blood pressure. AE not reported.	BMI, BMI SDS. Weight for height. AE not reported.	BMI SDS, body fat and waist. AE not reported.
Attrition	48% at 6/12, 73% at 12/12	2% at 2 yrs., 3% at 3 yrs.	23% at 6 months

Study	Lloyd-Richardson et al., 2012	Margarey et al., 2011	Mårild et al., 2012
Participants	110 OW 30-90% over BMI children (13-16 yrs) from clinic and community.	OW pre-pubertal children (5-9.9 yrs) recruited from the community.	64 OB children (8-13 yrs), 34 lean, 29 OW children and 138 OB children with no treatment recruited from clinics.
Study design	RCT comparing addition of exercise to behavioural intervention. No PC.	RCT to compare effect of including parenting programme in healthy lifestyles programme. PC given.	12-month RCT of two lifestyle interventions compared to no-treatment. PC given.
Intervention	Behavioural intervention of 16-week duration-included nutrition (portion control, healthy swaps, 1400-1600 calories), physical activity prescription (min 30 mins x 5 per week), self-monitoring, goal setting, stimulus control & relapse prevention. Also 4 x biweekly maintenance group sessions + 3-monthly activities. One group received weekly supervised exercise sessions; the other did weekly adventure therapy (Outward Bound).	6-months of lifestyles programme focused on nutrition & education sessions (8 sessions 90-120 mins. + 4 telephone sessions) OR parenting group (12 sessions 90-120 mins + 4 telephone sessions) focused on encouraging parents to manage high-risk situations relating to energy balance. Both were parent only-groups with optional active childcare.	Primary care delivered treatment aimed to support stepwise change to activity and nutrition. 12 sessions x 60 mins, Nurse-dietitian treatment arm (8 sessions with nurse +4 with dietitian with 10 on individual basis and 2 as groups) versus nurse-dietitian-physiotherapist treatment (4 sessions of each). Physiotherapist component focused on increasing activity using stepwise approach and incentives.
Underlying theory	Not stated.	Parent as the agent of change.	Motivational interviewing, CBT (goal setting, self-monitoring and reinforcement).
Outcomes	BMI SDS, %OW, self-concept and self-efficacy. AE not reported.	BMI SDS, waist, parenting questionnaires. AE=0.	BMI SDS, waist, laboratory tests. AE not reported.
Attrition	21% at 12/12, 25% at 24 /12.	6/12, /12 24/12: 17%, 24% and 36% in lifestyles and 14%, 31%, 39% in parenting.	13% at 12-months

Study	Moens et al.. 2011	O'Connor et al.. 2011	Okely et al.. 2010
Participants	50 OW (adjusted BMI>120%) children + 36 lean controls (6-12 yrs) recruited through healthcare.	40 OB (BMI 85-99th centile) children (5-8 yrs) from clinics.	165 OW children (5-10 yrs) with mean BMI SDS 2.8 from community.
Study design	12-month RCT of parend-led intervention or waiting list. No PC.	RCT of primary care intervention versus usual care. PC present.	6-month community-based RCT to compare 3 parallel group (diet+activity [n=70] programme against diet [n=63] or activity [n=73] only). Computer based allocation.PC present.
Intervention	Lifestyle education (increasing knowledge of nutrition and physical activity) and parent skills training (feeding, family functioning-supervision, house rules and discipline). Six group sessions of 2hrs delivered over 5-months.	Trained health advisors met with families individually once per month + follow-up phone all 2-wees later over 7 months. During session parents self-selected one behaviour to target: more vegetables, eat healthy snacks, eat more fruit, watch less TV, and drink more water). Involved goal setting and self-monitoring. Control group visited paediatrician as usual.	6-month programme. Weekly 2-hr session for 10 weeks with homework + monthly booster by telephone for 3 months. Parking vouchers and travel expenses reimbursed for participants.
Underlying theory	Social interaction theory.	Social cognitive and parenting theories	Health belief model + competence motivation theory.
Outcomes	Weight, feeding change, parenting. AE not reported.	Feasibility, BMI SDS, child behaviour (physical activity. Dietary intake, sedentary behaviour) and parenting. AE not reported.	Measured at 6 & 12 months. BMI SDS. Waist, blood pressure, lipids, physical activity. AE not reported.
Attrition	8% at 6/12 & 18% at 12/12.	15% at 7 months.	31% at 6/12, 36% at 12/12.

Study	Pedrosa et al.. 2011	Raynor et al.. 2012a	Raynor et al.. 2012b
Participants	83 OW (BMI>95th) children (7-9 yrs) from community.	101 OW (>85th centile) children (4-9 yrs) recruited from community & clinic.	81 OW (>85th centile) children (4-9 yrs) recruited from community & clinic.
Study design	12-month RCT comparing individual treatment with group treatment (3:1 randomisation). PC present.	RCT to compare growth monitoring alone or growth monitoring + parent intervention. Sealed envelope randomisation. PC present.	RCT to compare growth monitoring alone or growth monitoring + parent intervention. Sealed envelope randomisation. PC present.
Intervention	Promotion of lifestyle change in both. IT (baseline, 3, 6 and 12 months) prescribed 1800 kcal daily allowance (reduced intake of refined carbohydrates and saturated fats, increased fruit and vegetables, increased activity and reduced sedentary time. Group (4 sessions of 60 mins and follow up at 3,6, and 12 months) addressed healthy eating, healthy cooing, portion size, and food labelling and physical activity promotion.	Growth monitoring (monthly newsletter with information about healthy eating and activity behaviour. and letter with growth results) + biweekly 45min group parent sessions x 8 to reduce snack food and sugary drinks to less than 4/week plus increasing fruit (2 servings/day), vegetables (3 servings/day) and low-fat dairy (2 servings/day).	Growth monitoring (monthly newsletter with information about healthy eating and activity behaviour. and letter with growth results) + biweekly 45min group parent sessions x 8 to reduce sugary drinks to less than 4/week and increasing activity (to 60mins/day) plus increasing low fat dairy (2 servings/day) and reducing TV watching (<2 hrs. /day).
Underlying theory	Not stated	Goal setting, problem solving, stimulus control and parental modelling.	Goal setting, problem solving, stimulus control, parental modelling & behavioural economics
Outcomes	BMI SDS, laboratory tests, physical activity. AE not reported.	BMI SDS & dietary intake. AE=0	BMI SDS, dietary intake and leisure-time behaviour, AE=0
Attrition	17% at 6/12, 26% at 12/12.	8% at 6/12, 12% at 12/12	12% at 6/12, 10% at 12/12

Study	Reinehr et al.. 2010	Reinehr et al.. 2009	Sacher et al.. 2010
Participants	76 OW (BMI>90th<97th centile) children (8-16 yrs) reruited via media and GP practice. 32% low SES, 45% medium SES.	288 ob children 910-16 yrs) from clinic.	116 OB (>98th centile) children (8-12 yrs). Clinics and self-referral.
Study design	RCT comparing 6-month group programme (n=34) with waiting-list control (n=32). PC present. Computerised randomisation.	RCT comparing lifesytle programme to control group who could not attend programme. No PC.	RCT comparing community-based intervention to waiting list control. PC present.
Intervention	Counselling for nutrition physical activity and behaviour change x 37 sessions for children, 6 for parents and 5 for both (67 hrs. total). Activity was 90mins/weekx6 months, traffic light system for nutrition. 3 month intensive phase meeting weekly followed by monthly individual sessions x 3 months.	12-month outpatient programme of group nutrition sessions for children and parents (x6 x 90mins) + 6 months of individual family therapy (30min/month) + 3 months of weekly exercise sessions (available for 12-months).	18x2 hr. group educational and physical activity sessions held twice per week (8 focusing on behaviour change, 8 providing nutrition education and 16 activity sessions) + 12-week free swimming pass.
Underlying theory	Solution focused therapy + optimized mixed diet.	Optimised mixed-diet.	Social cognitive theory and study of therapeutic processes.
Outcomes	BMI, waist, body fat, blood pressure, dietary intake, sports activity, sedentary time, and socioeconomic status. Includes cost measure. AE=0	BMI SDS, waist, metabolic syndrome, blood pressure. AE not reported.	BMI, waist, body fat, physical activity, fitness and self-esteem. AE=0.
Attrition	9% drop out.	10% at 12-months.	29% at6/12, 31% at 12/12.

Study	Savoye et al. 2011	Stark et al 2011	Steele et al 2012
Participants	209 OB (BMI>95th centile) children (8-16 yrs) recruited from clinic.	18 OB (BMI>95th centile nut <100% over median BMI) children (2-5 yrs) recruited from clinic.	93 OW/OB (>85th BMI centile) chidlren (7-17 yrs) recruited from clinic & community.
Study design	RCT comparing family-based intervention to clinic care. PC present.	RCT comparing home-based behavioural intervention to enhanced usual care. No PC.	RCT comparing family-based group intervnetion with brief family intervention. PC present.
Intervention	Intervention group received lifestyle programme twice weekly for 6 months (exercise twice per week +, nutrition and behaviour modification x 1 per week), then twice monthly for 6 months Clinic control received counselling every 6 months.	6-month intervention: 12 weekly sessions (6 in child's home and 6 in group sessions) followed by group or home sessions ever 2 weekly for 12 weeks. Sessions included dietary and physical activity education + child behaviour management skills training + 14-day supply of vegetables supplied + child game and tasting group sessions. Home sessions addressed the application of education in the home. Usual care: paediatrician met with patient for 45 mins of prevention plus (<2hrs of screen time, 60 mins per day of active play, eliminating soda and reducing juice to 4oz/day, >5 servings of fruit and vegetables/day limiting eating out and appropriate portion sizes.	Positively fit: 10-weekly 90 min sessions for children & parents addressing behaviour change, nutrition, and activity. BFI families received Trim Kids: 3x60 min individual sessions with a dietitian over 10 weeks.
Underlying theory	Goal setting, cognitive-behavioural strategies.	Social cognitive theory	AMA guidelines
Outcomes	BMI, BMI SDS, laboratory tests, blood pressure. AE not reported.	BMI, BMI SDS, parenting, diet, quality of life. AE not reported.	BMI SDS, quality of life. AE not reported.
Attrition	22% at 6/12, 32% at 12/12	94% at 6/12 and 12/12.	38% at 12/12.

Study	Tjonna et al.. 2009	Wafa et al.. 2011	Wake et al.. 2009
Participants	54 OW/OB adolescents from clinic.	107 OB (BMI>95th centile) children (7-11 yrs) from community.	258 OW/OB (>90th centile but with a BMI SDS<3) Children (5-10 yrs) attending paediatric practices.
Study design	12-month RCT comparing multi-disciplinary treatment to aerobic intercal training. PC present.	6-month RCT of group treatment versus waitling-list control. PC present.	RCT comparing primary care treatment of obesity to control (educational letter). PC present.
Intervention	1x 3-min nutritional advice session + aerobic training was 3 months of walking/running uphill (40 mins: 4x4 min intervals at 90-95% max heart rate with 3-min recovery between intervals + 10-min warm up+5-min cool down. on a treadmill x 2/week. Training 1/fortnight for 6/12 and 1/month for 3/12. Group treatment was 21 hrs. In 3 months targeting activity (x3sessions) and nutrition.	Group treatment (8 hours contact over 26 weeks) aiming to change child sedentary behaviour, physical activity, and diet using behaviour change counselling. Parents had education while children participated in activity. Waiting list received intervention 6-months later.	GP visits x 4 over 12 weeks using a family folder addressing hydration, cutting down on fatty foods, increasing activity, decreasing sedentary behaviour and family eating habits (age 12 reading level).
Underlying theory	Not stated.	Social cognitive theory and transtheoretical model.	Solution focused therapy.
Outcomes	BMI, fitness, laboratory tests. Physical activity. AE not reported.	BMI, BMI SDS, physical activity, quality of life. AE not reported.	BMI, physical activity, costs and parent and child questionnaires. AE not reported.
Attrition	50% at 12/12.	25% at 6/12.	6% at 12/12.

Study	Wake et al.. 2013	Weigel et al.. 2008
Participants	118 OB (>95th centile but with a BMI SDS<3) Children (3-10 yrs) attending paediatric practices in Sydney.	73 OW children (>90th BMI centile) aged 7-15 years from clinic.
Study design	RCT comparing shared care to usual care control. PC present.	RCT comparing group (n=37) program with control (n=36). No detail on randomisation or PC.
Intervention	1x60 min tertiary care appointment (paediatrician & dietitian)	Outpatient nutrition program targeting physical activity, nutrition and coping (2 sessions per week in local sports club (1 for activity) + monthly parental sessions. Group used self-monitoring and goal setting. Control received written information from doctor after baseline visit.
Underlying theory		Not stated
Outcomes	BMI SDS, Body fat. Waist, physical activity, diet, self-esteem and parent BMI. AE not reported.	BMI, fat mass, blood pressure, laboratory tests. AE not reported.
Attrition	9% at 12/12	4% at 6/12, 10% at 12/12.

Table 2.2 Characteristics of studies included in the systematic review of mHealth interventions for childhood obesity

Study	*Participants*	*Study design*	*Underlying theory*
De Niet et al. 2012	144 children (8-12 yrs) who were overweight or obese (no definition)	Multi-centre RCT comparing texting intervention with control. PC given and t-testing used for analysis. Randomised by sealed envelope.	Social learning & self-regulation theory
Deforche et al. 2005	20 children who were obese and who had completed 10 months of an inpatient obesity intervention	RCT comparing maintenance programme 6 weeks after inpatient treatment finished. Control group did not receive contact. Every 2nd child randomised from a list. No PC given. Repeated mesures ANOVA for analysis.	Not stated
Estabrooks et al. 2009	220 parents of overweight children (>85th BMI centile) (8-12 years).	RCT to compare family workbook; workbook plus two group dietetic sessions or workbook, dietetic group sessions plus 10 interactive voice response sessions. ITT analysis used. PC given.	Social-ecological theory with health-centred approach & parent as agent of change.
Patrick et al. 2013	101 12-16 year olds with BMI > 85th percentile + two risk factors for T2DM	12 month RCT comparing website only, website + group and SMS or usual care. PC given. Randomized to	Behavioural determinants model & transtheoretical model of behaviour change
Nguyen et al. 2012	151 Overweight (BMI z score 1.0-2.5); 13-16 yrs. With access to a landline telephone and e-mail and/or a mobile telephone.	RCT comparing a two-phase behavioural lifestyle intervention with or without additional therapeutic contact (ATC) in Phase 2 for 12 months. PC given.	Cognitive behavioural approach
Nguyen et al. 2013	As in Nguyen 2012. In phase 2, 73 in group with ATC and 78 without.	Randomised to receive behavioural lifestyle intervention with or without ATC in Phase 2 for 24 months. No PC	Cognitive behavioural approach

Study	Intervention	Outcomes	Attrition
De Niet et al. 2012	Intervention group given mobile phone and intervention delivered x 9 months. Used tailored messaging based on the promotion of social support, motivation, reinforcement of positive change and suggestion of self-management skills + reminders after 1 week of non response	BMI SDS, PA, Sedentary & eating behaviour, quality of life and self-perception. No reports of AE.	30% in interventi on,, 31% in control.
Deforche et al. 2005	Weekly contact between therapist & patient by mail or phone. Bi-weekly phone calls to discuss activity behaviour during week 1-15 & 1 call every 3 weeks for last 6 weeks. Support & advice tailored to individuals. Patient encouraged to monitor physical & sedentary activity and update therapist each week. Goals encouraged via rewards.	Weight regain trajectory, physical Activity & sedentary behaviour.	Not reported.
Estabrooks et al. 2009	Promoting physical activity & fruit & vegetable consumption & reduce sedentary behaviour. Weekly group dietetic sessions x 2 hours. Focus on parental skills & knowledge of nutrition, physical activity, problem solving, strategies to modify the home environment & role-playing. IVR sessions commenced 1 week after the 2nd session. Parental response & branching logic used to determine call content.	BMI Well being, eating disorders, fruit & veg consumption,, physical activity.	38% workbook, 34% classes, 36% class + IVR..
Patrick et al. 2013	Intervention delivered in 3 phases over 51 weeks covering: education on healthy behaviours, interactive activities/games and goals. UC were encouraged to attend 3x 60-min group nutrition sessions. Cell phones and prepaid text message plans	BMI SDS, body fat, Physical Activity, food frequency, quality-of-life & self-esteem.	9% in interventi on and 11% in UC.
Nguyen et al. 2012	In phase 1 participants receive Loozit group program (7 x 75-minute weekly group sessions); phase 2 (2-24 months), adolescents attend booster group sessions every 3 months during each school term. In addition, adolescents in Loozit and ATC receive ATC during phase 2 every 2 weeks (telephone coaching, e-mails, and/or short message service text messages).	BMI SDS, waist to height ratio, metabolic outcome, PA, sedentary time, food frequency, psychosocial & adverse events	12% interventi on group and 23% in control.
Nguyen et al. 2013	Phase 1 (as in Nguyen 2012) phase 2 (2-24 months), adolescents continue to attend booster group sessions approximately once every 3 months during each school term. In phase 2, group randomized to ATC or no ATC.	BMI SDS, metabolic outcome, PA, sedentary time, food frequency, psychosocial & adverse events.	41% interventi on group and 36% in control.

3 CARDIOMETABOLIC CO-MORBIDITY IN CHILDHOOD OBESITY

3.1 Abstract

Background: Childhood obesity is associated with comorbidities, which can increase a child's risk for cardiometabolic disease. The prevalence of comorbidity is of particular importance in those who are morbidly obese.

Aim: This study aimed to estimate the prevalence of cardiometabolic co-morbidity including: hypertension, metabolic syndrome and insulin resistance in a consecutive series of children referred to a national tertiary paediatric obesity centre. Additionally the study aimed to describe the extent to which cardiometabolic abnormalities increase as obesity increases.

Methods: The study involved a sample of 267 children who were prospectively recruited from Temple Street Children's University Hospital in Dublin, Ireland. A standard physical and laboratory examination were carried out including measurement of blood pressure, height, weight, and fasting blood tests. Obesity was defined as having a body mass index (BMI) above the 98th centile for age and gender. Hypertension was defined based on paediatric guidelines. Insulin resistance was defined as having a homeostatic model assessment value above 2.5 and paediatric metabolic syndrome was defined using Weiss criteria. Children were classified according to severity of obesity and the prevalence of comorbidity was compared across obesity class.

Results: Eighty-five percent (n=227, 132 girls) of a consecutive series of patients were included in the study group. Children who did not complete blood testing (n=40, 15%) were excluded from the analysis. The mean BMI was 31.9 kg/m^2 (95% CI 31.1 kg/m^2, 32.7 kg/m^2), mean BMI SDS was 3.2 (95% CI 3.2, 3.3) and mean BMI centile was 99.8 (95% CI 99.7, 99.9). Hypertension was identified in 48.5% (95% CI 39%, 58%); the metabolic syndrome was present in 15% (95% CI 10.8%, 20.6%), and insulin resistance in 66% (95% CI 57.5%, 73.1%). In addition, hyperglycaemia was present in 10.3% (95% CI 6.2%, 16.4%) and glycated haemoglobin levels indicated a risk of diabetes in 2.8% (95% CI 0.8%, 7.1%). Approximately one

percent (95% CI 0.1%, 4.2%) of the group met the criteria for type-2 diabetes mellitus. With increasing BMI, there were statistically significant increases in the prevalence of hypertension (p=0.01), metabolic syndrome (in boys p=0.03) and hyperglycaemia (in girls, p=0.03).

Conclusion: Children who are obese present with multiple cardiometabolic co-morbidities that should be urgently addressed.

Keywords: metabolic syndrome; obesity; paediatric; insulin resistance; hypertension; co-morbidity.

3.2 Background

Childhood obesity has now become a major problem in Ireland with 19% of children overweight and 7% obese at nine years of age (7). Childhood consequences of obesity include early signs of cardiovascular and metabolic disease, low physical fitness, musculoskeletal impairments and high blood pressure (21, 25, 128, 149, 152, 185). Similarly, children who are obese have a greater likelihood of persistent obesity into adulthood and a greater risk of cancer, Type 2 diabetes and cardiovascular disease in adulthood (186-188). A recent meta-analysis of studies describing cardiovascular risk factors in children concluded that children who were obese had higher blood pressure; higher blood lipids; more insulin resistance and greater increases in left ventricular mass compared to children within the 'healthy' range for body mass index (BMI)(55). The multiple comorbidities associated with childhood obesity are depicted in Figure 3.1.

Worryingly, metabolic syndrome also presents in children who are obese (27). Reaven described the metabolic syndrome as "a link between insulin resistance, hypertension, dyslipidaemia, impaired glucose tolerance and other metabolic abnormalities associated with an increased risk of atherosclerotic cardiovascular diseases in adults" (189). Studies of Irish youth who are obese have reported low insulin sensitivity, reduced exercise tolerance, low levels of physical activity, especially vigorous activity and high levels of sedentarism (190-192). To date, however the presence of the metabolic syndrome in Irish children has not been described. Given that cardiometabolic health and obesity in childhood can influence rates of chronic adult disease, it is essential that those with a high risk for such diseases are identified and managed appropriately.

3.3 Aims

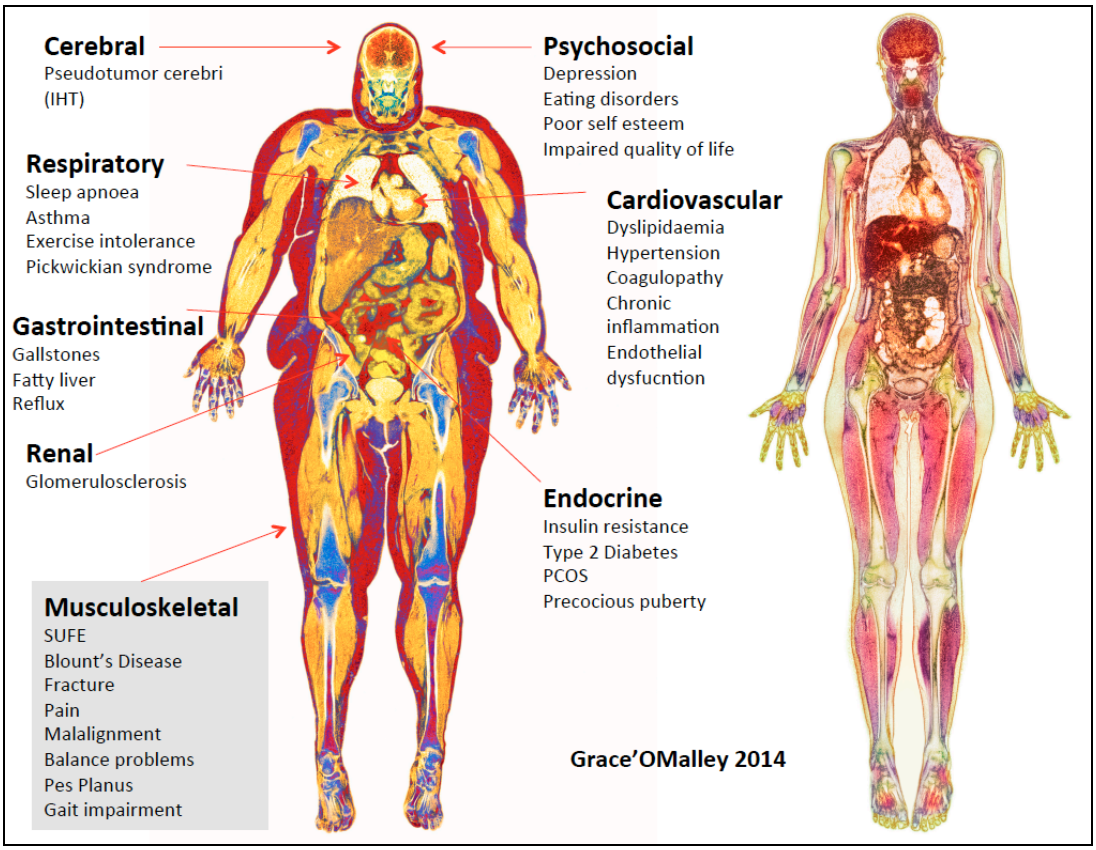
The aims of the study were:

- To estimate the prevalence of hypertension, the metabolic

syndrome and insulin resistance in a consecutive series of children referred to a national tertiary paediatric obesity centre.

- To describe the extent to which cardiometabolic abnormalities increase as obesity increases.

Figure 3.1 Co-morbidities associated with childhood obesity



3.4 Methods

3.4.1 Study design

The study was a cross-sectional audit of children prospectively recruited from a national tertiary paediatric obesity centre between 2007 and 2013. The study was completed in accordance with the Declaration of Helsinki and ethical approval was granted by the ethics committee of the Temple Street Children's University Hospital (130701).

3.4.2 Participants

The Temple Street Paediatric Obesity Service in Dublin, Ireland is a national multi-disciplinary tertiary care service for children and adolescents who are clinically obese (193). Children are referred mainly from an area of urban disadvantage and were recruited for the study if they had a BMI ≥98thpercentile, if they were aged 3-16 years and if they completed a standard laboratory test. Children with a known-diagnoses (Type-1 diabetes or syndromic cause of obesity) were excluded. Figure 3.2 describes a participant flow-chart through Study 2 and Study 4.

3.4.3 Assessment

At initial assessment a standard physical and laboratory examination were carried out including measurement of blood pressure; height, weight, and fasting blood tests: glucose (FPG); insulin (FI); alanine aminotransferase (ALT); aspartate aminotransferase (AST); triglycerides (194); total cholesterol (Chol); low and high-density lipoprotein cholesterol (LDL, HDL) and glycated haemoglobin (HbA1C).

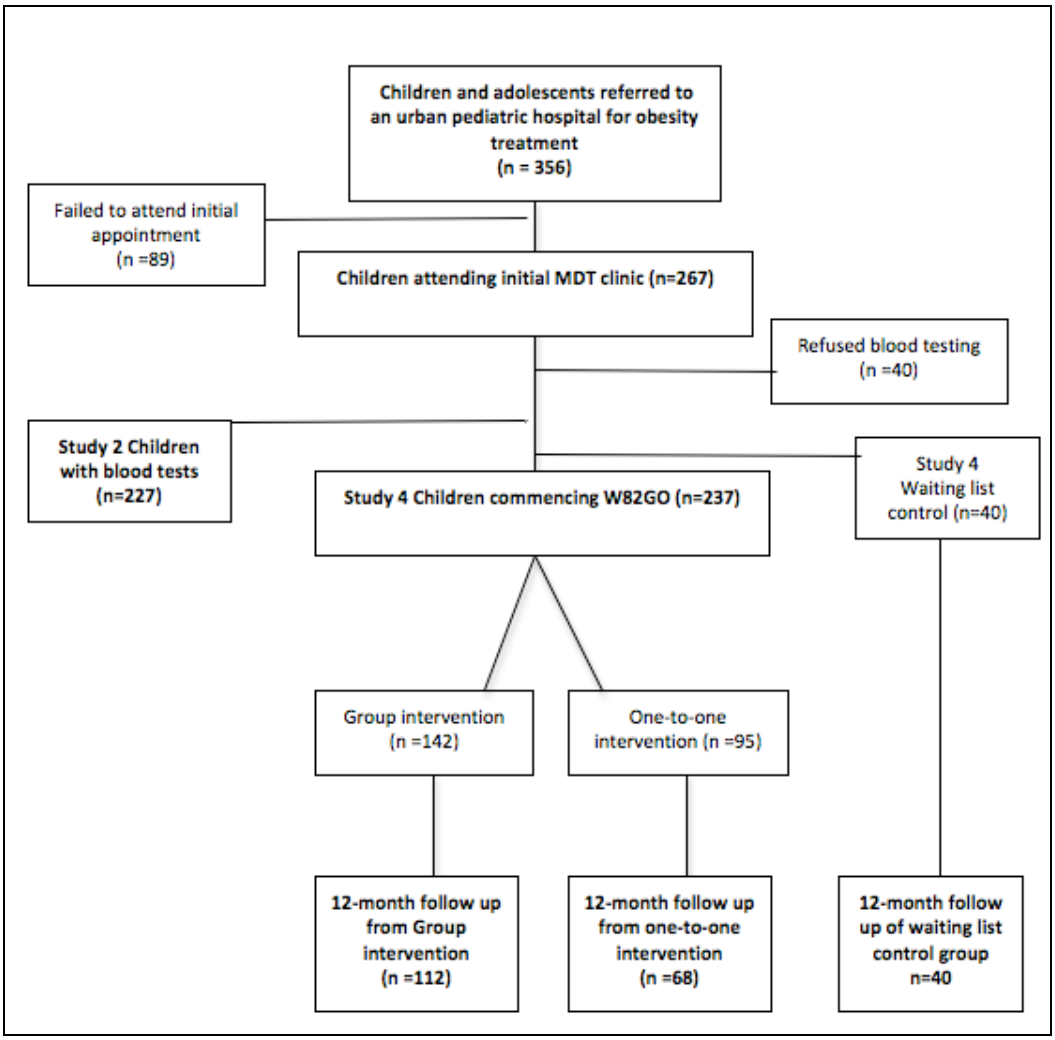
3.4.4 Outcome measures

3.4.4.1 Anthropometry

Weight was measured (with participant in socks with no shoes and wearing light clothing) in kilograms to the nearest 0.1 kg using a medical weight scale (SECA, model 952, Germany), zeroed and calibrated before each weighing. A wall-mounted stadiometer (Harpenden, Cambridge, Md), calibrated in 0.1 cm intervals, was used to determine height. Both height and weight were measured in triplicate and the average value calculated. BMI was calculated (kg/m^2) and BMI SDS and BMI percentiles were calculated using the LMS method (195). Children were classified as having: Class 1 Obesity if BMI SDS was 2.0 and 2.49; Class 2 Obesity if BMI SDS was 2.5-2.99; Class 3 Obesity if BMI SDS was 3.0-3.49 and Class 4 Obesity if BMI SDS was over 3.5. The study group was divided into two age groups: those under

12 years and those between 12 and 16 years.

Figure 3.2 Flow-chart of patients through Study 2 and Study 4 of PhD



3.4.4.2 Blood pressure and laboratory tests

Blood pressure (BP) was measured by a single observer using an OMRON sphygmomanometer (OMRON 705CP-II, Kyoto, Japan) after five minutes of rest in the sitting position. All readings were taken in the left arm. Appropriately sized cuffs were used with cuff-width 40% of mid-arm circumference, and cuff bladders covering 80-100% of the arm

circumference and approximately two thirds of the length of the upper arm without overlapping. The measurements were taken in triplicate and the average of the second and third measurement was recorded. Blood pressure percentiles (BP perc) for age and gender were calculated according to paediatric guidelines (196). Pre-hypertension was defined as a systolic and/or diastolic BP perc between the 90th and 94.9th percentile and hypertension was defined as a systolic and/or diastolic BP perc greater than or equal to the 95th percentile. If participants were identified as pre-hypertensive or hypertensive they were advised to visit their general practitioner to confirm the readings on two separate occasions.

3.4.4.3 Metabolic syndrome

The metabolic syndrome was defined according to Weiss (27). Children who met three or more of the following criteria were classified as having the metabolic syndrome: a BMI SDS of 2.0 or more; triglycerides >95th centile for age and gender; HDL lower than the 5th centile for age and gender; and a systolic or diastolic blood pressure >95th percentile for age and gender.

3.4.4.4 Metabolic calculations

The homeostasis assessment model for insulin resistance (HOMA-IR) formula was used as an index of insulin resistance (fasting insulin (mU/mL) × fasting glucose (mmol/L)) / 22.5. A HOMA-IR >2.5 was defined as insulin resistance (197). The triglyceride/high density lipoprotein ratio (Tg/HDL) is a good indicator of insulin resistance in children who are obese and was calculated by dividing triglyceride values (mg/dl) by HDL values (mg/dl)(198).

3.4.5 Statistics

All statistical analyses were performed using SPSS version 20 (IBM Inc. Chicago, USA). Descriptive statistics were completed and variables that were not normally distributed were log transformed. Differences between gender and the obesity classes were estimated using analysis of variance and a

general linear model with adjustment for gender and age was used to estimate differences across classes of obesity. Chi square tests were used to determine the relative number of children who presented with cardiometabolic abnormalities and metabolic syndrome across classes of obesity. The 95% confidence intervals for binomial proportions were calculated using the modified Wald method (199).

3.5 Results

3.5.1 Participants

Between 2007 and 2012, 267 children attended for clinic assessment. Fifteen percent (n=40) did not complete blood testing as children refused to have blood drawn due to anxiety and/or expectation of pain. Children who did not have blood testing were less obese than those who did complete testing (BMI SDS of 2.8 ± 0.32 versus 3.2 ±0.58, p=0.04). Therefore, there were 227 children in the study cohort (132 girls).

3.5.2 Outcomes

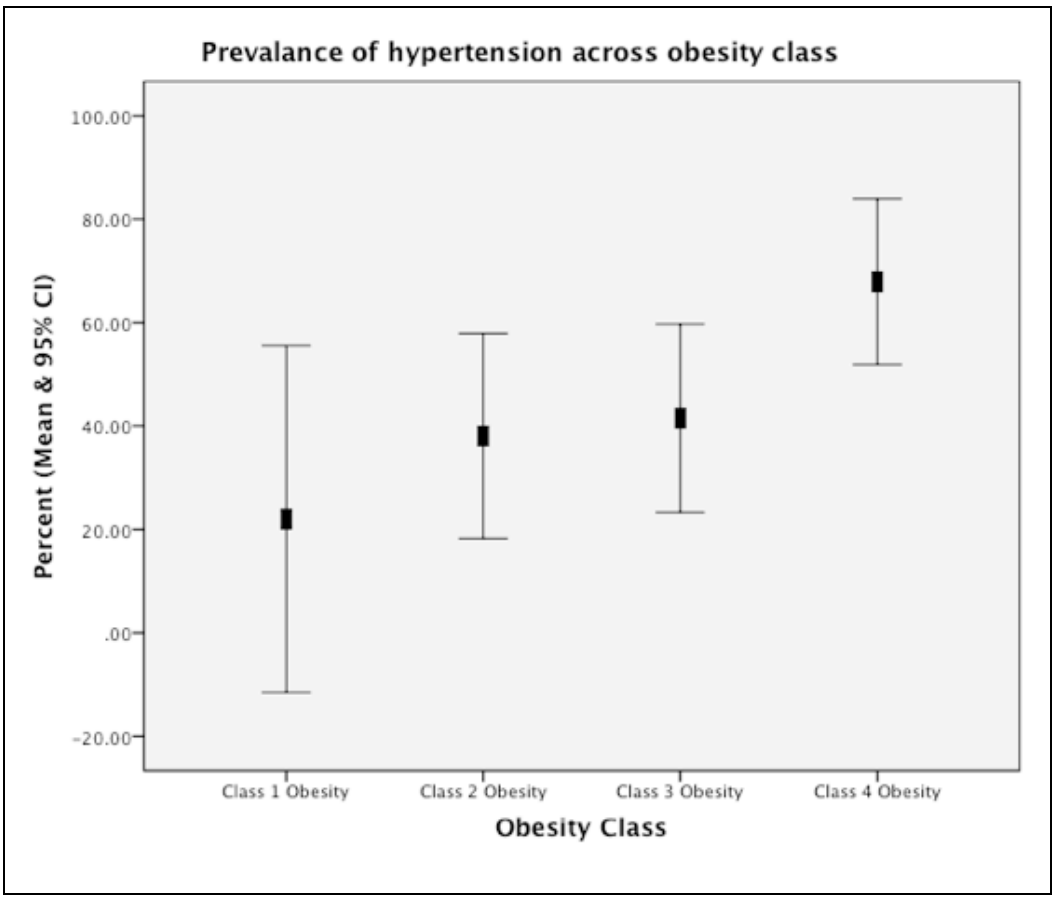
3.5.4.1 Anthropometry

Table 3.1 describes the baseline characteristics of the cohort. There were no gender differences observed for these variables. Twenty-three children (13 girls) were class 1 obese, 63 children (36 girls) were class 2 obese, 64 children (33 girls) were class 3 obese and 75 children (49 girls) were class 4 obese.

3.5.4.2 Blood pressure and laboratory tests

Blood pressure values are presented in Table 3.2. An increase in blood pressure values was observed across obesity classes but this was not significant when adjusted for age and gender. Pre-hypertension and hypertension were identified in 11 children (10.9% [95% CI 6%, 18.6%]) and 49 children (48.5% [95% CI 39%, 58%]) respectively. Hypertension increased as obesity level increased as depicted in Fig 3.3.

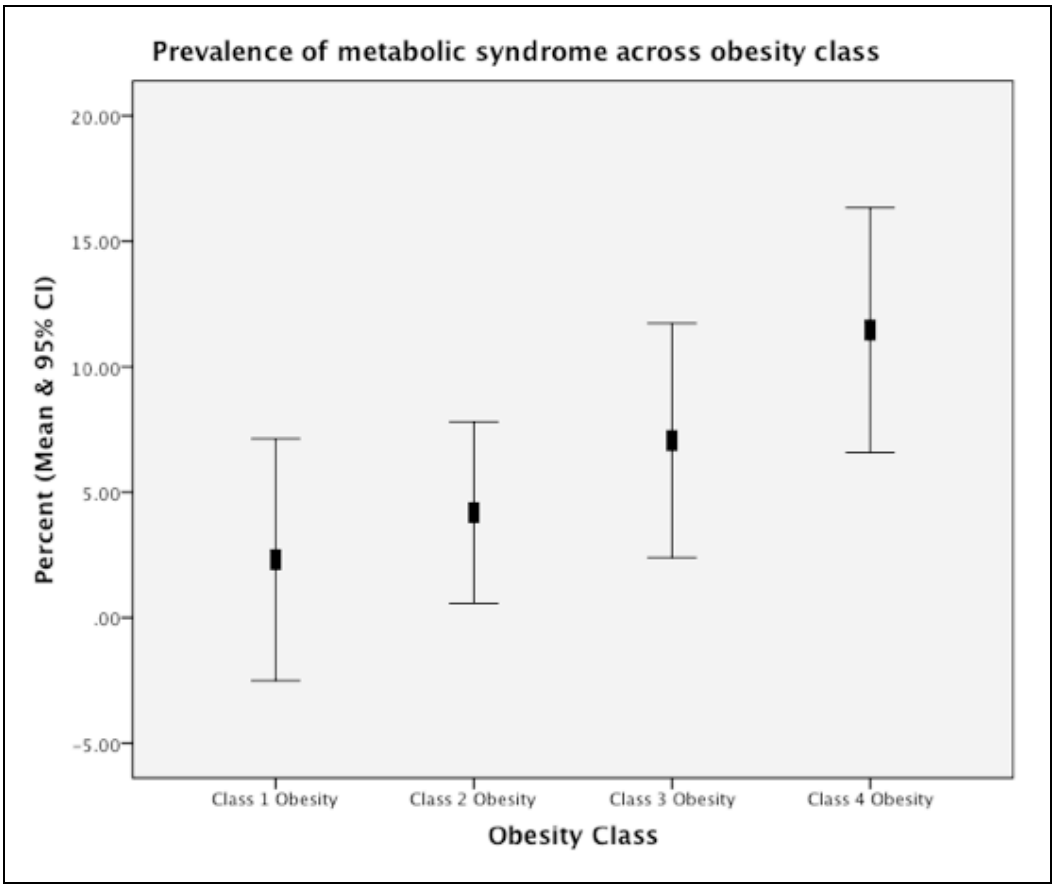
Figure 3.3 Prevalence of hypertension across obesity class[1] in children attending a paediatric obesity service



[1]Increase in prevalence of hypertension as obesity level increased (χ=15.64, p=0.02).

When adjusted for age and gender, significant differences were seen across obesity class for triglycerides (F=5.93, *p*=0.003), HDL (F=4.1, *p*=0.009), ALT (F=4.56, *p*=0.01) and insulin (F=5.05, *p*=0.002). Table 3.1 describes the observed abnormalities from laboratory tests. As obesity increased, there was a trend for greater prevalence of abnormal blood results though this was only significant for high total cholesterol (χ=7.84, *p*=0.049), for high LDL (χ=12.85, *p*=0.005), for hyperinsulinaemia (χ=8.76, *p*=0.033) and in younger children for high ALT levels (χ=9.82, *p*=0.02).

Figure 3.4 Prevalence of metabolic syndrome across obesity class[1] in children attending a paediatric obesity service



[1]Increase in prevalence of metabolic syndrome was significant for boys only (χ=8.7, p=0.03).

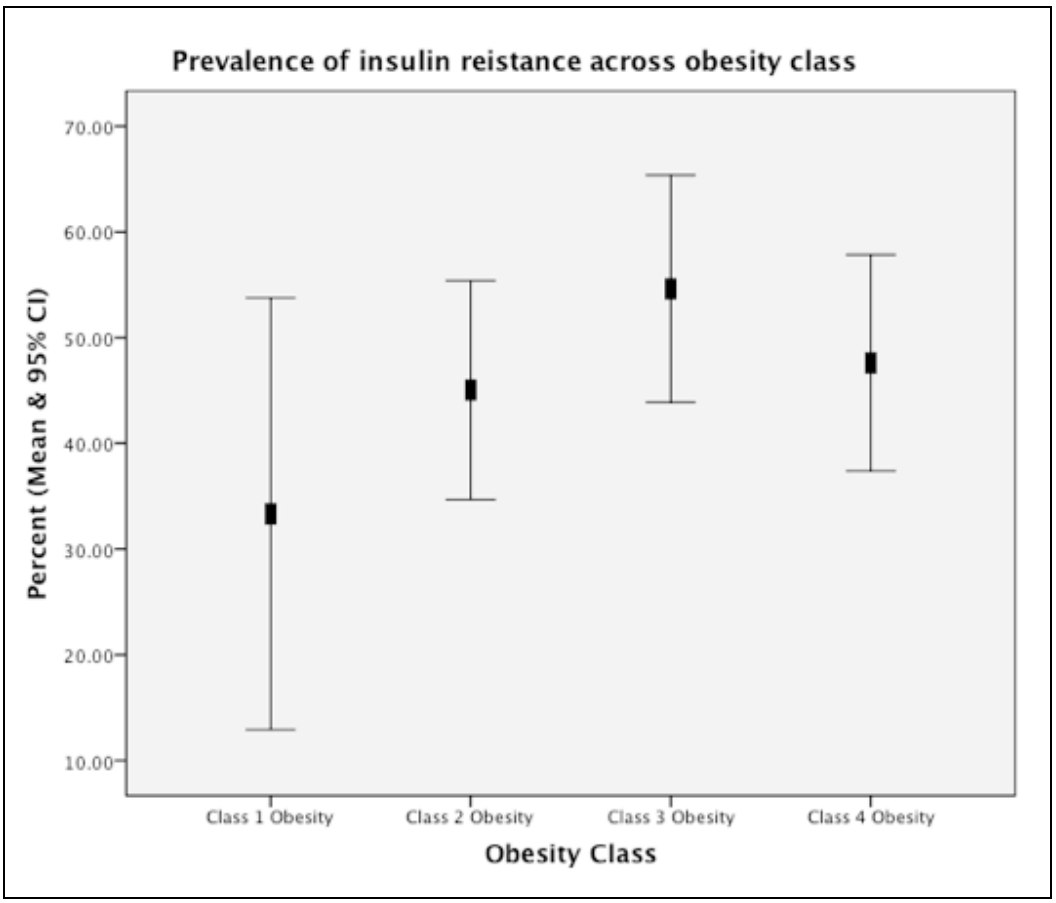
3.5.4.3 Metabolic syndrome

From 207 children, 31 (15% [95% CI 10.8%, 20.6%]) met the criteria for having the metabolic syndrome (20 girls). The prevalence increased across classes of obesity from 4.7% in class 1 obesity (95% CI <1%, 2.4%) to 24% in class 4 obesity (95% CI 15.2%, 34.7%) as shown in Fig. 3.4.

Children with the metabolic syndrome had higher BMI (34.72 kg/m^2 [95% CI 32.5, 36.9] versus 31.7 kg/m^2 [95% CI 30.8, 32.6], p=0.009) compared to those without it. In addition, they had higher levels of fasting insulin (204.29

[95% CI 152.8, 255.8] versus 105.10 [95% CI 90.1, 119.7], p<0.001), TG/HDL ratio (4.4 [95% CI 3.8, 5.1] versus 1.90 [95% CI 1.7, 2.1], p<0.001) and HOMA-IR (7.85 [95% CI 5.8, 9.9] versus 4.1 [95%CI 3.3, 4.7], p<0.001) compared to those without the syndrome.

Figure 35 Prevalence of insulin resistance across obesity class[1] in children attending a paediatric obesity service



[1]IR increased from 46.7% in Class 1 obesity (95% CI 24.8%, 69.9%) to 66.7% in Class 4 obesity (95% CI 52%, 78.7%) but was not statistically significant.

3.5.4.4 Metabolic calculations

Table 3.2 presents the mean values and 95% CI for metabolic calculations across obesity class. A high proportion of children (66% [95% CI 57.5%, 73.1%]) had a HOMA-IR >2.5 and were diagnosed with insulin resistance (IR). There was a trend for IR to increase as obesity increased (see Fig 3.5). Children with IR were older (12.5 versus 9.2 years, p<0.001), were taller (141.9 cm versus 156.4 cm, p<0.001), were heavier (85.7 kg versus 61.0 kg, p<0.001) and had higher BMI (33.2 kg/m^2 versus 28.3 kg/m^2, p<0.001) compared to those with a HOMA-IR <2.5. An abnormal TG/HDL ratio was observed in 45.8% (95% CI 35.5%, 56.5%) of the group and the prevalence of a high TG/HDL ratio increased from 25% (95% CI 6.5%, 59%) in class one obesity to 48% (95% CI 30.7%, 66%) in class four obesity. Children with high TG/HDL were heavier (82.4 kg versus 69.7 kg, p=0.02) compared to those with a normal TG/HDL ratio.

3.6 Discussion

This study estimated the prevalence of hypertension, the metabolic syndrome and insulin resistance in a sample of clinically obese youth being treated in a national paediatric obesity centre in Ireland. The children referred to clinic are mainly from the hospital catchment area (an area of severe to extreme urban disadvantage) and may not be representative of the typical child who is obese in Ireland. Similarly, the study sample excluded children who refused to complete a blood test, which may have introduced an element of bias to the study. Children did not want to complete a blood test due to anxiety and the expectation of pain and this is an important finding for the phlebotomy and obesity services. Future work is needed to improve communication around the importance of blood testing and to explain to patients that pain is minimised by use of local anaesthetic cream.

Hypertension was observed in over 40% of participants. As blood pressure was taken on one occasion only for this study, the results should be considered with caution. This observation is supported however, by data

from the U.K. where 32% of children attending an obesity clinic were hypertensive(200). Recently an analysis of 117,618 children aged 6–17 years attending well-child visits found that children who were severely obese (BMI ≥120% × 95th percentile) were at 2.7-fold greater odds of hypertension compared to those who were moderately obese (BMI 100-119% (201). Furthermore Babinska et al reported an increasing risk of ambulatory hypertension as obesity increased in children 7-18 years. Nearly 50% of the participants with hypertension suffered from severe ambulatory hypertension (202).

We estimated a 15% prevalence rate of the metabolic syndrome in our group. We did not include an estimate of glucose tolerance in the classification of metabolic syndrome, as children attending our national service do not routinely undergo an oral glucose tolerance test as part of their initial clinic assessment. The rate of metabolic syndrome we observed is lower than reported prevalence estimates from other paediatric clinical groups (19% in Germany, 25% in the U.K., and 28% in the U.S.A)(203-205). Such differences in prevalence rates may be due to the different age ranges, levels of obesity, and races included in other studies. Whether such clustering of risk factors in childhood can predict cardiometabolic disease more effectively than the risk of each individual component remains unknown and warrants further study.

We described insulin resistance in 66% of children. As we did not compare HOMA-IR against a group of lean children we cannot determine whether changes were due to rising obesity or purely increasing age. However we attempted to address this limitation by adjusting for age and gender in our analysis. We also reported that 45% of children had an abnormal TG/HDL-C ratio (>2.7). Children with a TG/HDL-C ratio of greater than 2.27 are more likely to present with insulin resistance as measured by oral glucose tolerance testing (198) and this measure may be a quick method of estimating risk of metabolic disease. Longitudinal study of these outcomes and exploring whether or not they can be reduced with standard treatment

is urgently needed.

These findings are in agreement with the published literature. In a systematic review of 34 moderate to high-quality studies, Reilly et al., (206) observed that childhood obesity was consistently associated to the presence of: hypertension; dyslipidaemia; abnormalities in endothelial function; impaired left ventricular mass/function and hyperinsulinaemia and insulin resistance. We could not compare the prevalence of cardiometabolic burden in our group compared to a group of lean children. However, work by Freedman et al. indicated that the odds ratios for having a clustering of two and three cardiometabolic risk factors in obese 5-10 year olds were 9.7 and 43.5 respectively compared to children who were not obese (207).

Our second aim was to determine the extent of the increment in cardiometabolic abnormalities as level of obesity increases. We observed a rising prevalence of hypertension and metabolic syndrome in tandem with rising values of insulin resistance across obesity, which has been observed elsewhere. These increases highlight the importance of providing timely treatment for children who are severely obese however should be considered with caution as the sample size was small and the study was not powered statistically. Nevertheless, treating severe obesity at an early age is important given the high rates of co-morbidity and given that in adults, those with severe obesity have twice the risk of death from all-cause mortality compared to those with moderate obesity (208). Similarly, our observations that nearly 3% of the group was at risk of type 2 diabetes and that 1% already met the criteria for type 2 diabetes are important findings, which represent significant implications for individual children but also for the health service.

We observed dyslipidaemia in nearly 35% of children with results similar to that of other clinical studies (200). These data are worrying given the association between abnormal blood profiles and development of insulin resistance, non-alcoholic fatty liver disease, and cardiovascular disease (25,

209-211). Our study provides reliable estimates regarding the prevalence of cardiometabolic disease in a group of children who are obese. However, at the level of the individual child this data should be considered with caution.

We report a concomitant increase in cardiometabolic co-morbidities as obesity increases and this may be related to the development of ectopic fat deposits. Fat tissue deposited in visceral, intramuscular, hepatic and subcutaneous compartments is linked to the development of inflammation, insulin resistance and deranged glucose metabolism (128, 212-214). We did not measure body composition in the current study and further research will be required to explore the relationship between ectopic fat and cardiometabolic co-morbidities in children. Such co-morbidities are in addition to a slew of other obesity-related physical and psychosocial co-morbidities including musculoskeletal pain, higher rates of fractures, depression and low self-esteem. Recent data describes that such co-morbidities can be reduced with conservative lifestyle treatment (215, 216). Therefore, it is vital that children who are obese receive timely effective treatment in an effort to ameliorate such childhood comorbidities and prevent further progression to adult disease.

3.7 Conclusion

Children who are obese present with a multitude of cardiometabolic co-morbidities, which can affect their health in childhood and increase their risk of chronic disease. The prevalence of these comorbidities increases as obesity level rises. It is essential that access to effective evidence-based interventions is available to all children with a diagnosis of clinical obesity.

3.8 Acknowledgements

Sincere thanks to the phlebotomy department in Temple Street Children's University Hospital for the kindness and care shown to participants undergoing blood testing. The candidate is responsible for the study design, data collection, data analysis and writing of the paper.

Table 3.1 Prevalence of abnormal laboratory values in children attending for weight managment

Cardiometabolic abnormality	*Sample size*	*Prevalence (mean and 95% CI)*
Hypercholesterolaemia	212	33.85% (27.5%, 40.8%)
High LDL	95	7.06% (3%, 14.8%);
Low HDL	95	23.46% (15.5%, 33.8%);
High triglycerides	200	32.59% (26.2%, 39.7%)
Hyperglycaemia	228	10.3% (6.2%, 16.4%)
Hyperinsulinaemia	152	16.4% (10.8%, 24.1%);
High ALT	162	16.4% (11.6%, 22.6%)
High AST	162	5.6% (2.9%, 10.2%)
Hba1c levels indicated risk of type 2 diabetes	155	2.8% (0.8%, 7.1%).
Hba1c levels indicating presence of type 2 diabetes	155	1% (0.1%, 4.2%).

Table 3.2 Anthropometric characteristics of participants attending TSCUH for weight management (n=227)

	All children n=227	*<12 years n=109*		*>12 years n=118*	
		Boys n=63	Girls n=46	Boys n=46	Girls n=72
Age (years)	11.7 (11.3,12.1)	9.2 (8.6,9.9)	8.9 (8.4,9.5)	14.1 (13.7,14.5)	14.0 (13.7,14.3)
Height (cm.)	152.1 (149.9, 154.4)	141.5 (137.,145.6)	139.1 (134.6,143.7)	166.9[1], (164.8,169.1)	160.6 (158.5,162.7)
Weight (kg.)	77.6 (74.1,81.1)	57.1 (52.8,57.89)	60.5 (54.3,66.6)	94.7 (89.7,99.8)	94.9 (89.9,99.7)
BMI kg/m^2	31.9 (31.1,32.7)	27.9 (26.8,29.1)	29.2 (27.7,30.6)	34.1 (32.6,35.5)	35.5 (34.2,36.7)
BMI SDS	3.23 (3.15,3.30)	3.32 (3.24,3.25)	3.26 (3.11,3.42)	3.13 (2.99,3.26)	3.21 (3.09,3.33)
BMI Centile	99.8 (99.8,99.9)	99.8 (99.7,99.9)	99.8 (99.7,99.9)	99.8 (99.7,99.9)	99.8 (99.7,99.9)

[1] In older children, boys were taller than girls ($p<0.001$)

Table 3.3 Cardiometabolic characteristics of children attending TSCUH for weight management classified by level of obesity

	All children	*Class 1 obese*	*Class 2 obese*	*Class 3 obese*	*Class 4 obese*	*P value*
n		10	27	33	39	
Systolic BP[1] (mm Hg)	123 (121,126)	116 (107,126)	121 (116,125)	123 (119,128)	123 (124,124)	0.1
n		10	27	33	39	
Diastolic BP[2] (mm Hg)	77 (75,79)	76 (66,86)	73 (70,76)	77 (74,77)	80 (76,84)	0.1
n		8	28	20	27	
Tg/HDL ratio	2.47 (2.16,2.79)	1.43 (0.51,2.35)	2.28 (1.82,2.74)	2.86 (2.11,3.60)	2.71 (2.12,3.30)	0.01[3]
n		15	46	34	45	
HOMA-IR	4.78 (3.63,5.94)	3.55 (1.48,5.61)	3.98 (3.0,4.95)	6.23 (4.35,8.11)	4.68 (3.62,5.73)	0.01[4]

[1]Younger children presented with lower systolic (120.1 [116, 124.2] versus 125.9 [122.9, 128.8] for older children, p=0.02)

[2]Younger children presented with lower diastolic values (75.9 [72.5, 79.3] versus 77.5 [77.3, 80.2] for older children, p=0.50)

[3] With adjustment for age and gender F=3.94.

[4] With adjustment for age and gender F=4.4.

4 THE ROLE OF BODY COMPOSITION: DOES CHANGE PREDICT METABOLIC FUNCTION?

4.1 Abstract

Background: The use of body mass index in childhood is limited and additional measures of body composition are recommended in order to estimate risk of disease during childhood. Additionally, changes in body composition are associated with changes in metabolic health in adults, but few data exist for children. Body composition is often measured using dual-energy X-ray absorptiometry (DXA) however; DXA exposes children to radiation and is costly. Recently, bioelectrical impedance analysis (BIA) has been proposed as a potential substitute method for estimating body composition. BIA does not expose children to radiation, is cheaper and does not require specially trained operators.

Aim: This study aimed to establish the validity of substituting BIA for DXA when estimating body composition in a clinical group of adolescents who are obese. In addition we sought to investigate whether changes in body composition predicted change in insulin sensitivity over time.

Method: This observational study examined 112 adolescents to determine agreement between the DXA and BIA methods for estimating percent fat, fat mass and fat free mass. Bland and Altman plots and Pearson correlations were used to compare BIA to DXA as the reference method. In addition, 28 adolescents completed a hyperinsulinaemic-euglycaemic clamp to measure insulin sensitivity at baseline and 12-month follow up. Linear regressions (with adjustment for baseline BMI SDS and gender) were used to test whether changes in body composition estimated using both methods could predict changes in insulin sensitivity over time.

Results: BIA measures were significantly correlated with DXA for each of the measures of body composition (Pearson coefficients of 0.69 ($p<0.001$) for percent fat 0.92 ($p<0.001$) for fat mass (FM) and 0.90 ($p<0.001$) for fat free mass (FFM). However, Bland-Altman plots of the differences between the two methods revealed poor agreement. For the estimation of PF, BIA measures could be 15.9% lower or 5.6% higher than estimates from DXA.

For FM, BIA measures could be 17% lower or 5.8% higher than estimates from DXA and for FFM; BIA measures could be 8.7% lower or 13.9% higher than estimates from DXA. Over time changes in insulin sensitivity were significantly predicted by changes in fat mass, fat free mass and percent fat as measured by both methods.

Conclusions: In a clinical cohort of children who were obese, BIA gave poor estimates of body composition compared to DXA. However, both methods of body composition predicted changes in insulin sensitivity over time. BIA which is does not involve radiation could be used in obesity clinics to track body composition and indicate change in insulin sensitivity in settings where DXA is unavailable.

Keywords: body composition, percent fat, fat-free mass, and insulin sensitivity

4.2 Background

Accurate assessment of body composition in adolescents is essential if obesity treatment and prevention approaches are to be evaluated effectively. The gold standard technologies for in vivo body composition assessment are magnetic resonance imaging and X-ray computed tomography scanning, though neither is appropriate for routine monitoring. Other measurement options range from simple techniques such as: skin-fold thicknesses; waist circumference; and body mass index (BMI) to more involved techniques including: densitometry; isotope dilution; dual energy X-ray absorptiometry (DXA); and bioelectric impedance analysis (BIA). Clinically, overweight status in children is commonly measured using body mass index (BMI) as a proxy, though this variable does not differentiate between body fat and more metabolically active lean body mass (217). Furthermore, BMI yields no information regarding the distribution of body fat, and as ectopic fat deposition is associated with an increased risk of cardiometabolic disease (218, 219) alternative techniques that detail body composition may be more useful in clinical practice.

The use of DXA and BIA is controversial in paediatric populations (220-222). DXA exposes children to radiation, is costly, requires a large amount of space and paediatric-specific software and measurement takes approximately 20 minutes. BIA is less costly, portable does not expose children to radiation, take five minutes to complete but has significant ceiling and floor effects. Though each method has its advantages and disadvantages, it is important that measurement of body composition be accurate on an individual basis. Accurate classification of body fat distribution may assist in estimating the risk of developing future diseases (194, 223). A number of studies have investigated the relationship between body composition and cardiometabolic health whereby, in adults, BIA measures of fat tissue have been shown to correlate weakly with metabolic risk factors (224). Percent body fat (measured with air-displacement plethysmography) has been suggested to be no better than BMI and waist

circumference for detecting metabolic risk in the general adolescent population (225), however data in obese cohorts are sparse.

4.3 Aim

This study aimed to establish the validity of substituting BIA for DXA when estimating body composition in a clinical group of adolescents who are obese. In addition we sought to investigate whether changes in body composition predicted change in insulin sensitivity over time.

4.4 Methods

4.4.1 Participants

Participants who were obese (BMI>95th percentile) and who spoke English fluently were recruited from the Yale Obesity and Lipid Disorders Clinic. Females who were pregnant were excluded from participation. Having completed the age-appropriate parental consent and child assent forms, participants were invited to attend the Yale Clinical Research Center for evaluation. All procedures were in line with the Helsinki Declaration of 1975 (as revised in 1983).

4.4.2 Outcomes

4.4.4.1 Anthropometry and body composition

Weight was measured (with participant in socks with no shoes and wearing a light gown) in kilograms to the nearest 0.1 kg using a medical weight scale (model CN20, Detecto, a division of Cardinal Scale Manufacturing Co, Webb City, Mo), zeroed and calibrated before each weight. A stadiometer (Harpenden, Cambridge, Md), calibrated in 0.1-cm intervals, was used to determine height. BMI was calculated (kg/m^2) and obesity was defined according to U.S. cut-offs (BMI equal to or above the 95th percentile). Participants underwent baseline body composition assessment and a convenience sample completed a hyperinsulinaemic-euglycaemic clamp as

previously described (226). Measures of body composition (PF, FM and FFM) were determined by DXA with a Hologic scanner (Boston, MA) using standard mode and paediatric software and by BIA (Tanita, TBF 300, Tanita Corp of America, Inc., Arlington Heights, Ill).

4.4.4.2 Metabolic function

Participants underwent baseline body composition assessment and a convenience sample completed a hyperinsulinaemic-euglycaemic clamp as previously described (226). Insulin sensitivity was calculated from clamp data yielding values for insulin sensitivity (M), which were adjusted for lean body mass (LBM) as previously described (227). Body composition and metabolic function were repeated at 12-month follow up.

4.4.4.3 Agreement between body composition measured by DXA and BIA

Bland and Altman plots and Pearson correlations were used to compare measures of body composition estimated with BIA and DXA methods. Differences between sample characteristics and metabolic outcomes were compared using t-testing or Mann-Whitney U testing where appropriate, and changes over time were compared using pair-wise testing.

4.4.4.4 Tracking metabolic changes over time with changes in body composition

Linear regressions were used to test the association between change in body composition variables and change in metabolic outcomes, with adjustment for baseline age and BMI SDS and gender.

4.5 Results

4.5.1 Participants

One hundred and twelve youths (45 male, 26 peri-pubertal) were examined at baseline and 59 were re-measured at follow up to determine agreement between body composition measures. Children with follow-up measures of DXA/BIA were not different at baseline compared to those who did have

follow-up measures taken.

4.5.2 Outcomes

4.5.4.1 Anthropometry and body composition

Participant characteristics are detailed in Table 4.1. At baseline, boys were taller (p=0.12) than girls. There was no baseline differences between boys who had follow-up body composition measures compared to those without follow-up. Girls with repeat body composition measures were younger at baseline compared to those without follow-up (13.42 years [12.63-14.22] versus 14.98 years [14.34-15.62], p=0.003).

4.5.4.2 Metabolic function

At baseline and 12-month follow up 28 children [11 boys] completed a hyperinsulinaemic-euglycaemic clamp. Girls with follow up clamp were younger than those without follow up (13.30 years [12.11-14.29] versus 14.57 years [13.96-15.18], p=0.03). Adolescents who had a repeat clamp had greater baseline BIAFFM at baseline compared to those who did not have a follow up clamp (see Table 4.2). Over time significant increases were seen for fat mass (FM) measured with DXA (p =0.004 for adolescents with repeat clamp) and for fat-free mass (FFM) measured using both methods (p <0.001 for adolescents with repeat clamp). Table 4.3 describes the clamp-derived metabolic outcomes at baseline and follow up. There were no significant differences between measures for boys and girls at baseline or follow-up using t-tests. Paired t-testing revealed that height, weight and BMI increased significantly between baseline and follow-up (p<0.001; 0.001 and 0.006 respectively).

4.5.4.3 Agreement between body composition measured by DXA and BIA

DXA and BIA measures were significantly correlated for all measures with Pearson coefficients of 0.69 (p<0.001) for PF, 0.92 (p<0.001) for FM and 0.90 (p<0.001) for FFM. However, the Bland-Altman plots of the differences between the two methods for the individual studies show poor agreement

between BIA and DXA for PF, FM and FFM (Figs. 5.1-5.3). For PF, the mean bias and 95% confidence intervals were -5.1 [-6.108, -4.108]; the lower limit of agreement and 95% confidence intervals were -15.70 [-17.43, -13.97] and the upper limit of agreement and 95% confidence intervals were 5.54 [3.81, 7.27]. The percentage error of PF measured with BIA compared to DXA was 52.6%, p<0.0001. For FM, the mean bias and 95% confidence intervals were -5.78 [-6.96, -4.60]; the lower limit of agreement and 95% confidence intervals were -17.40 [-19.43, -15.37] and the upper limit of agreement and 95% confidence intervals were 5.84 [3.81, 7.87]. The percentage error of FM measured with BIA was 61.1%, p<0.0001. For FFM, the mean bias and 95% confidence intervals were 2.60 [1.46, 3.74]; the lower limit of agreement and 95% confidence intervals were -8.68 [-10.63, -6.73] and the upper limit of agreement and 95% confidence intervals were 13.88 [11.93, 15.83]. The percentage error of PF measured with was 41.9%, p<0.0001.

4.5.4.4 Tracking metabolic changes over time with changes in body composition

Table 4.4 describes the results from the correlations between change in body composition and change in metabolic variables. The mean (95% CI) number of months between first and second measures was 17.35 (13.03, 21.67). Significant negative correlations were seen between change in body composition measures and change in measures of metabolic function. The correlations were not appreciably different between the two measures used thus changes in the BIA and DXA measures tracked the metabolic changes reasonably well. Table 4.5 describes the linear regression models whereby the P values indicate the significance for the body composition covariate used in each model. The changes observed for insulin sensitivity (M and M/LBM) were tracked significantly by changes in body composition as measured by both DXA and BIA. Specifically, each unit change in M was predicted by unit changes in PF (0.09 by DXA and 0.14% by BIA) and FM (0.10g by DXA and 0.09g BI). Each unit change in M/LBM was predicted by unit changes in PF (0.28% by DXA and 0.21% by BIA), FM (0.18g by DXA and 0.17g BIA), and FFM (0.23g by DXA and 0.20g BIA).

Figure 4.1 Bland-Altman plot for agreement on percent body fat measures between DEXA and BIA methods

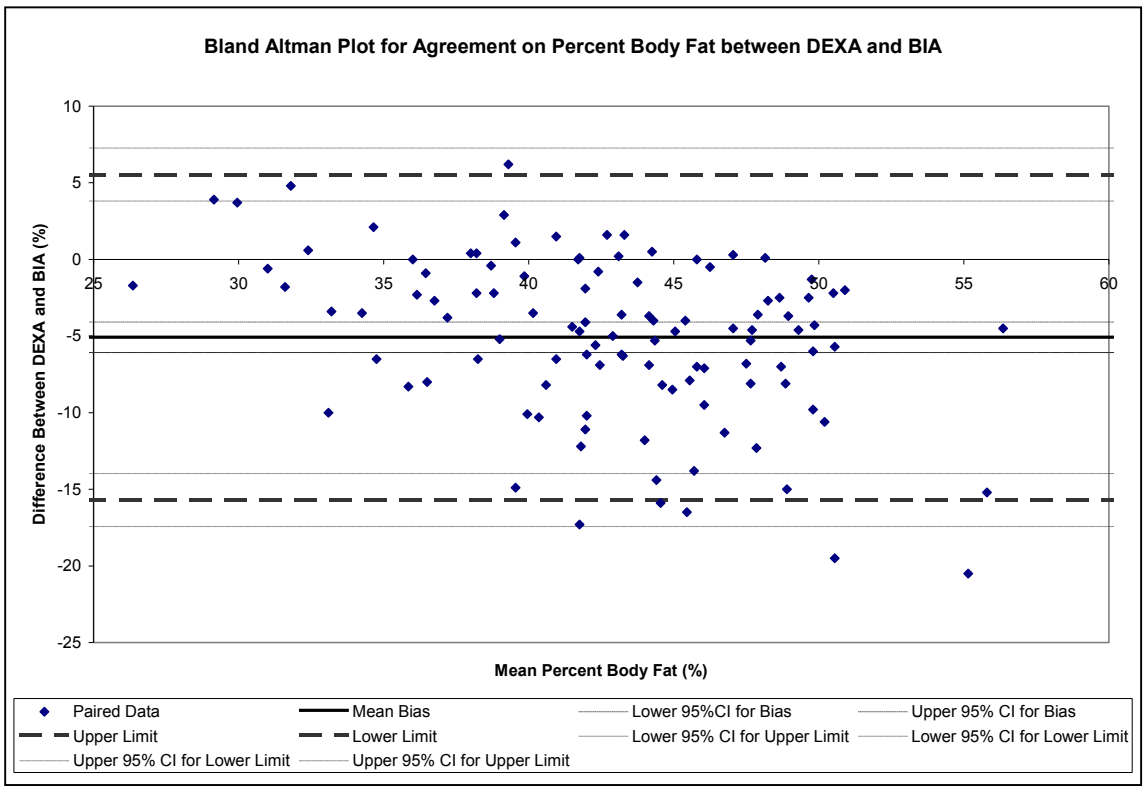


Figure 4.2 Bland-Altman plot for agreement on fat mass measures between DEXA and BIA methods

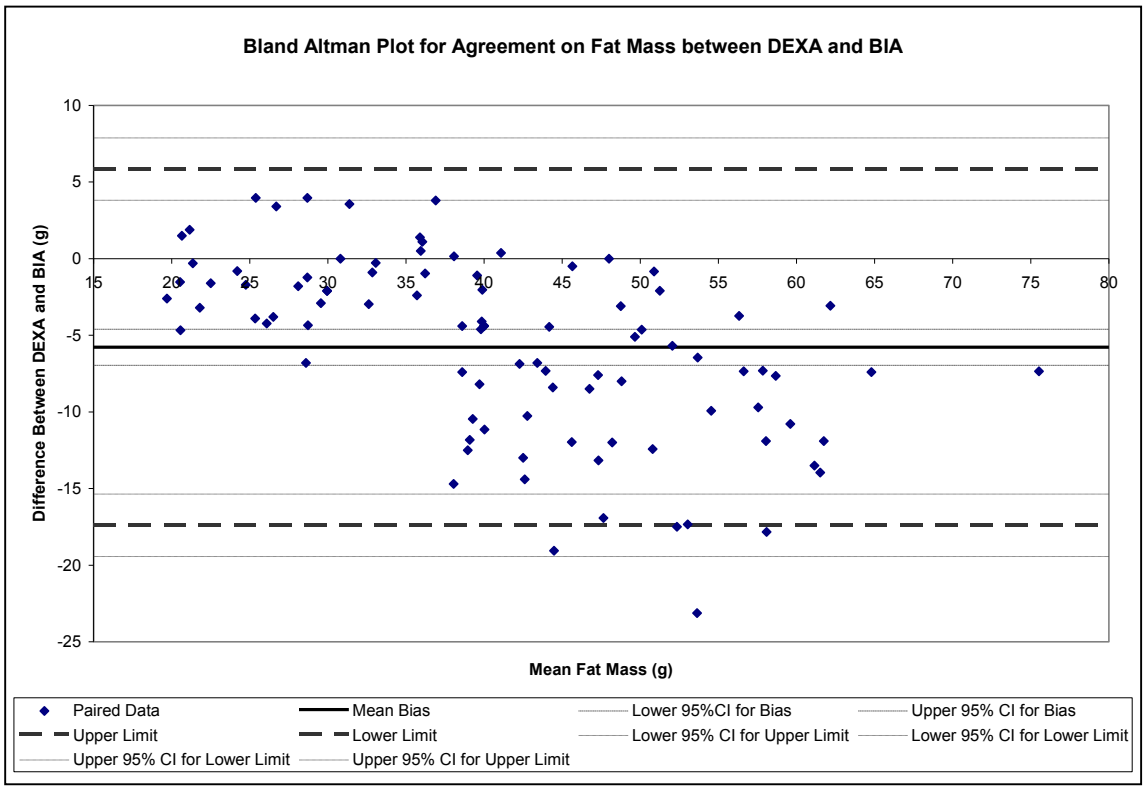
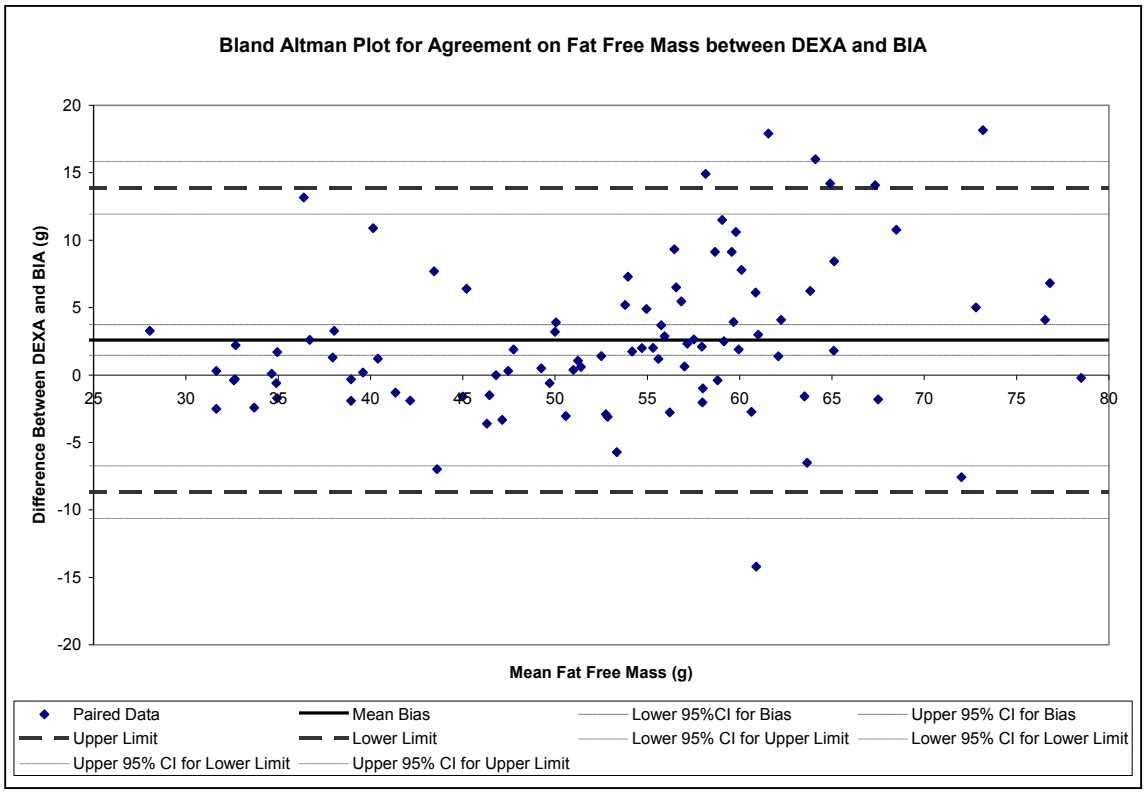


Figure 4.3 Bland-Altman plot for agreement on fat free mass measures between DEXA and BIA methods



4.6 Discussion

Our study aimed to establish the validity of using BIA to measure body composition as compared to DXA at a reference method, in a clinical cohort of obese adolescents. In addition the study examined whether body composition measures, could predict change in metabolic measures over time. In support of previous work in adults, DXA and BIA measures correlated reasonably well in our group of youth with obesity. However, using Bland and Altman methods, we found poor agreement, with large bias values (particularly in children who were more obese). Therefore, we would not recommend that BIA be used in replacement of DXA. Previous reports

describe systematic underestimation of body composition using BIA compared to DXA (228, 229). Our results support other work in child and adolescent cohorts, where errors in the estimation of body composition variables (e.g. FM) using DXA and BIA were large particularly in obese children and adolescents (220). There was a tendency for BIA to underestimate PF and FM as the values increased. It has been proposed that the in-built BIA Tanita equations do not accurately predict body composition across a variety of ethic groups (230) and work by Clasey et al. (231) has outlined the validity of using alternative predictions equations in the use of BIA in paediatric cohorts. Unfortunately when our study was being conducted, such equations were not available and as our study cohort was multi-ethnic our findings may have an inherent bias given the work by Haroun et al (230). Similarly, the participants in this study were drawn from a consecutive series of patients attending an obesity clinic, which may have introduced a selection bias. The results suggest that BIA should not be considered as a substitute for DXA for the measurement of body composition in children who are morbidly obese but that it might be useful for children who are less obese. Equally, it is important to note that the two methods should not be used interchangeably due to within-subject differences. Our group being exclusively obese and the lack of a control group are issues that limit the findings of our study.

Though achieving an accurate measure of body composition at a given point in time is important, in the second study aim, we sought to examine whether changes in body composition over time reflected a change in metabolic function over time, using either DXA or BIA. Data regarding how changes in body composition relate to changes in metabolic function are sparse, though work by Hemmingsson *et al.* (224) described a weak correlation between BIA estimates of PF and FM, and metabolic risk factors in adults (insulin, blood lipids etc.).

Pubertal status and ethnicity are reported to influence insulin sensitivity (232), however neither of these variables were significant predictors of

metabolic function in our regression analyses. Pubertal assessment in children is a highly sensitive area. Tanner staging in children and adolescents who are obese often causes distress, which can have a negative influence on patient engagement. As such, pubertal status in the study was estimated based on an age-related cut-off of 10 years. In future studies Tanner line drawings or hormonal levels (e.g. testosterone in boys) might be more appropriate methods of estimating and monitoring puberty without affecting patient engagement.

The study results describe correlations between change in body composition and change in measures of insulin sensitivity over time. Determining the influence of body composition on insulin sensitivity is challenged by the fact that our cohort was obese. Our finding that increasing FM and PF predicted reductions in insulin sensitivity (M; M/LBM; Mm2) is in agreement with a previous report by Brufani et al (233). This group observed that FM in obese girls and both FM and FFM in obese boys, were independent predictors of insulin sensitivity (adjusted for pubertal stage, adiponectin, leptin and IGF_1). Unlike the current study, which measured change in pubertal children only, Brufani *et al.* measured the variables through pubertal development. Similarly, work by Goran et al (234), reported that FM significantly predicted insulin sensitivity and the acute insulin response in a mixed group of white and African American children.

Adam and colleagues hypothesized that changes in insulin sensitivity and resistance in childhood are related to the development of fat mass later on in life (235). In their 2009 study, they reported that changes in insulin sensitivity at an early age influenced weight gain in the future and that changes in FM were not related to changes in insulin sensitivity measured by intravenous glucose tolerance testing. In our study we observed that changes in body composition were evident when the Gold-standard hyperinsulinaemic-euglycaemic clamp was used. Our finding that changes in FFM were negatively correlated to changes in insulin sensitivity is counter-intuitive but is in agreement with work by Brufani et al (233). This finding

warrants further study in a greater number of subjects and across a wider range of BMI classification. In our study, regression models showed a significant prediction of M/LBM by FFM measured by DXA in boys only (Beta=-2.0, R=0.87, *p*=0.046) and may reflect the greater number of fast muscle fibres (which are related to insulin resistance) in boys compared to girls (236).

Our study was limited, as we did not collect standardised information on levels of physical activity and physical fitness. These variables could have influenced body composition (in particular FFM) and indices of insulin sensitivity (237). It may be prudent for future studies to compare the predictive effect of various compartments of body fat on alterations in metabolic health. A unique strength of this study however, was the assessment of changes in body composition and metabolic measures longitudinally over time using Gold Standard techniques.

4.7 W82GO evaluation: conclusion

The W82GO intervention for childhood obesity was effective in reducing BMI SDS compared to a waiting list control group. Further research is warranted to measure the treatment effect on cardiometabolic outcomes. Data related to the cost-effectiveness of such treatment are also needed.

4.8 Acknowledgements

The candidate and Prof. Sonia Caprio conceived the study. Prof Sonia Caprio, Melissa Shaw, Bridget Pierpont, the candidate and Dr. Ram Weiss carried out the study. Data were analysed by the candidate, Prof. Sonia Caprio and Dr. Veronika Northrup of the Yale Clinical Centre for Investigation. The candidate drafted the paper and all authors reviewed the final version. Sincere thanks to all the study participants and their families for partaking in this work. This study was possible due to funding from grants to Prof Caprio from the national Institutes of Health (R01-HD04787 and R01-HD0208016) and by CTSA Grant Number UL1 RR024139 from the national

Center for Research Resources, a component of the national Institute of Health. Thanks also to The Fulbright Commission of Ireland for funds related to this study granted to the candidate.

Table 4.1 Baseline characteristics of participants included in study exploring agreement between BIA and DXA[1]methods of esimating body composition[1]

	Baseline sample with paired DXA/BIA measures n=112		***Sample with follow up DXA/BIA measures n=59***	
Ethnicity	AA=39, C=33, H=40		AA=20, C=18, H=21	
	Boys n=45	Girls n=67	Boys n=26	Girls n=33
Age (years)	13.5 (12.7,14.2)	14.2 (13.7,14.7)	13.8 (12.8,14.8)	13.4 (12.6,14.2)
Height (cm.)	165.0 (161.0,168.8)	159.2 (156.9,161.5)	167.0 (162.1,171.9)	157.1 (153.2,161.1)
Weight (kg.)	96.2 (89.3,103.2)	94.5 (89.4,99.7)	97.0 (88.2,105.8)	90.5 (82.7,98.2)
BMI (kg/m^2)	35.0 (33.2,36.8)	36.9 (35.4,38.5)	34.5 (32.2,36.7)	36.1 (34.1,38.2)
BMI SDS	2.43 (2.33,2.53)	2.35 (2.27,2.43)	2.38 (2.24,2.52)	2.37 (2.28,2.47)
BMI Centile	99.0 (98.7,99.3)	98.8 (98.5,99.0)	98.8 (98.4,99.3)	99.9 (98.6,99.2)

[1]Values presented are mean and 95% confidence intervals. African-American=AA, Caucasian=C, Hispanic=H.

Table 4.2 Baseline and 12-month follow-up body composition measures in study measuring agreement between BIA and DXA [1]

	Baseline sample with clamp plus DXA/BIA measures n=28		*Follow-up sample with clamp plus DXA/BIA measures n=28*	
	Boys	Girls	Boys	Girls
Age (years)	14.3 (12.2,16.4)	12.9 (12.0,13.9)	16.3** (14.3,18.3)	15.1** (13.9,16.3)
Height (cm.)	165.5 (156.4,174.5)	155.9 (150.0,161.8)	170.9* (163.2,178.6)	160.4* (155.4,165.4)
Weight (kg.)	97.7 (80.6,114.7)	86.9 (74.8,99.0)	106.1 (90.3,122.0)	97.8* (86.1,109.5)
Percent body fat	40.7 (38.7,42.7)	46.1 (43.7,48.7)	41.6 (38.6,44.6)	45.0 (41.7,48.3)
Fat mass	35.4 (31.0,39.7)	41.2 (35.2, 47.2)	42.5* (37.0,48.0)	45.5 (39.4,51.5)
Fat-free mass	49.9 (44.2,55.6)	46.6 (42.0,51.2)	54.9* (50.3,59.4)	53.7* (49.3,58.1)

*[1]Values presented are mean and 95% confidence intervals. *p<0.05, **p<0.01*

Table 4.3 Baseline and 12-month follow up measures of insulin sensitivity in study exploring whether changes in body composition could predict changes in insulin sensitivity[1]

Metabolic calculation	*Baseline sample with clamp n=28*		*Follow-up sample with clamp n=28*	
	Boys	Girls	Boys	Girls
Insulin sensitivity (m)	3.6 (1.6,3.6)	3.3 (1.6,5.0)	3.9 (1.6,6.2)	3.4 (1.9,5.0)
Insulin sensitivty/fat free mass (m/lbm)	165.5 (156.4,174.5)	155.9 (150.0,161.8)	170.9* (163.2,178.6)	160.4* (155.4,165.4)

*[1]Values presented are mean and 95% confidence intervals. *p<0.05, **p<0.01.*

Table 4.4 Bivariate correlations between body composition and sensitivity in study exploring whether changes in body composition could predict changes in insulin sensitivity

Metabolic calculation	*DXA n=28*			*BIA n=28*		
	Δ Percent Fat	Δ Fat mass	Δ Fat free mass	Δ Percent Fat	Δ Fat mass	Δ Fat free mass
Δ Insulin sensitivity (m)	-0.2	-0.5**	-0.3	-0.4*	-0.4*	-0.3
Δ Insulin sensitivty/fat free mass (m/lbm)	-0.3	-0.7**	-0.6**	-0.5**	-0.6**	-0.5*

**p<0.05, **p<0.01*

Table 4.5 Association between changes in body composition and insulin sensitivity in study exploring body composition measurement in paediatric obesity[11]

	DXA n=28			*BIA n=28*		
	Δ Percent Fat	Δ Fat mass	Δ Fat free mass	Δ Percent Fat	Δ Fat mass	Δ Fat free mass
Δ Insulin sensitivity (m)						
Beta	-0.09	-0.1	-0.1	-0.14	-0.09	-0.09
SE	0.09	0.03	0.05	0.06	0.03	0.07
R2	0.05	0.27	0.13	0.19	0.26	0.08
P value	0.32	0.01	0.08	0.03	0.02	0.20
Δ Insulin sensitivty/fat free mass (m/lbm)						
Beta	-0.18	-0.18	-0.23	-0.21	-0.17	-0.20
SE	0.12	0.04	0.07	0.09	0.04	0.09
R2	0.19	0.53	0.38	0.29	0.45	0.26
P value	0.15	0.001	0.001	0.02	0.001	0.04

[1]Linear regression adjusted for gender, baseline age and baseline BMI SDS. Standard error=SE, R-squared=R2.

5 W82GO HEALTHY LIFESTYLES SERVICE: DEVELOPMENT AND CLINCAL EFFECT OF A CHILDHOOD OBESITY INTERVENTION

5.1 Abstract

Background: Children who are clinically obese present with a range of physical and psychological co-morbidities and best-practice treatment aims to assess and treat these in order to improve child health and avoid chronic disease in adulthood. In order to deliver effective treatment to children and adolescents who are obese, it is essential that interventions are evidence-based and are fully described.

Aims: The first aim is to describe development and main components of the Temple Street W82GO Healthy Lifestyle's Programme (W82GO). The second aim is to evaluate the effect of W82GO on body mass index standardized deviation score (BMI SDS) at 12-months in children and adolescents who were clinically obese and to estimate the numbers needed to treat in order to achieve a clinically significant reduction in BMI SDS of 0.25.

Method: Part one of this chapter describes how an intervention mapping approach was used to develop the W82GO intervention. Part two describes a pre-post study of treatment effect: children (<16 years) with a BMI >98th centile who were referred to W82GO were offered treatment delivered over 12 months. Treatment was delivered as a group treatment or in the form of individual treatment. A group of 40 children on a waiting list served as a control group. Changes in BMI SDS between the two groups were compared in analysis adjusted for baseline age, gender, BMI centile and time between measurements.

Results: Part one of this chapter describes in detail the components and strategies used in W82GO and justifies the use of such components. In part two: 237 parent-child dyads commenced treatment (117 boys, 142 in GT) and attended for baseline assessment. In addition, there were 40 children in the waiting list control group (15 boys). Twelve-month data were available for 180 treated children (88 boys, 112 in group treatment), yielding dropout rates of 21% and 28% in GT and individual treatment respectively. When adjusted for baseline covariates, the overall change in BMI SDS was -0.18

(95% CI -0.23, -0.13) while in the control group BMI SDS increased by 0.05 (95% CI -0.04, 0.14) ($F=8.6$, $p<0.001$). The mean difference of group treatment and individual treatment compared to control were -0.23 (95% CI -0.36, -0.11) and -0.23 (95% CI -0.37, -0.10) respectively. The number needed to treat for a clinically significant reduction in BMI SDS was five for group treatment and six for individual treatment.

Conclusion: The W82GO intervention is a promising form of obesity treatment and future research is warranted to explore the effect on obesity and additional health-related outcomes via a randomized controlled trial.

CHAPTER 4 PART ONE
W82GO DEVELOPMENT

5.2 W82GO development: background

Childhood obesity is prevalent in the West and so too are the associated short- and long-term comorbidities. In Ireland, 19% of 9-year old children are estimated as overweight and 4-8% as obese (52, 238). In addition, in Ireland and elsewhere, higher rates of childhood obesity are associated with social disadvantage (238-242). Short-term consequences of obesity are prevalent and include joint pain; sleep apnoea, hypertension and endocrine dysfunction (21, 25, 128, 190, 243) and the negative effects of severe obesity on mood and self-esteem may have lifelong consequences. Children who are obese are also predisposed to the early development of cardiovascular risk factors (152). Long-term consequences include a greater likelihood of persistence of obesity into adulthood and a greater risk of cancer, Type 2 diabetes and cardiovascular disease (244). Given the burden of such consequences, it is imperative that evidence-based preventative and therapeutic strategies are implemented. Timely treatment is important as a child who is obese has a high probability of becoming an obese adult (245). There is sufficient evidence to justify well-targeted treatment of children with obesity and meta-analyses indicate that evidence-based treatment interventions can produce significant and clinically meaningful reductions in obesity (246). In response to the serious issue of childhood obesity, the author and members of a multi-disciplinary clinical team developed the Temple Street W82GO Healthy Lifestyles Treatment Service (W82GO).

5.3 W82GO development: aim

To describe the development and main components of W82GO based on an intervention mapping approach (247).

5.4 W82GO development: methods

Needs Assessment

5.4.4.1 Identifying the problem

In 2005, the author and a representative from the Temple Street Children's University Hospital departments of nursing and dietetics began to develop a childhood obesity intervention (W82GO). At the time there was no obesity treatment available in Ireland for children. At the time of writing W82GO remains as Ireland's only treatment option for children who are obese.

5.4.4.2 Identifying a solution

We used the IX Method for Grading Health Care Recommendations in order to explore the published evidence relating to childhood obesity treatment and the expected health-related effects (248). The initial development of W82GO from 2005-2007 was guided by identifying the evidence available at the time regarding the treatment of childhood obesity. Evidence included the report of the Irish National Task Force on Obesity and international paediatric clinical research (249-257). Between 2007 and 2011, W82GO was further developed as additional clinical guidelines from the UK (58), Scotland (258) and the USA (259) were published.

Guided by the NICE framework, W82GO integrated practices including: the development of a multidisciplinary team (consisting of a physiotherapist, a paediatrician, a nurse, a psychologist and a dietitian); the development of a dedicated clinic for children who are obese; the holistic assessment of readiness to change in families who attended for treatment; the development of a multi-component family-based intervention delivered in either an individual or group-based setting; the tailoring of education and advice to families based on their native language and levels of literacy; the offering of appointments outside normal clinical working hours; the integration of sessions to build on children's self esteem and self concept; and the use of standardized outcome measures to assess physical and psychosocial health.

In addition, advocacy work was undertaken to highlight the importance of childhood obesity assessment and treatment within the healthcare system and within Temple Street Children's University Hospital in particular. Similarly, research and audit practices were established to facilitate the on-going development of the intervention. Evidence suggests that positive, persistent results may be obtained through interventions which are family-based and combine cognitive-behavioural, nutrition and physical activity strategies in a lifestyle centred approach (258).

Formulation of change objectives

In keeping with best practice evidence, the overall aim of the W82GO intervention is to enable permanent change in a child's habits relating to eating behaviour, physical activity and sleep (258). Thus, the focus of treatment is not only on reducing obesity, but also rather on the behavioural and attitudinal changes required to establish and maintain a healthy lifestyle. Such lifestyle changes are determined by a number of performance objectives (e.g. such as a reduction of excessive consumption of energy dense foods) and the formulation of these objectives is agreed between the family, the child and the clinical team. Forming the required objectives is guided by behaviour change theory (260-263). The behaviours and attitudes of the family in relation to health promotion are identified during a thorough assessment (Appendix VII) and specific, tailored change objectives are developed (see Table 5.1). In order to achieve change in these variables a number of sub-behaviours are promoted, such as self-monitoring by the child and parent/s, self-management, goal setting and problem solving. At every opportunity the service aims to empower the family to recognise behaviours that could be changed and encourages development of the skills required to make and sustain such changes.

5.4.4.3 Initial Referral

When first established, W82GO accepted referrals from hospital consultants only. However, since 2012, direct referral from general practitioner and allied health professionals was introduced (see referral form in Appendix

VII). The transtheoretical model (stages of change model) is incorporated from the initial contact, when the service is described and the family's level of interest is assessed. In line with other areas of obesity treatment(264), the rate of non-attendance at initial appointment is high (25%) which may indicate the proportion of families at a less active phase of the change process (262). Attempts are made at this point to increase engagement and move families along the cycle of change by providing both verbal and written information on the clinical services and treatment available to them (see Appendix for the parent/child information material developed by the candidate).

5.4.4.4 Holistic Assessment

The initial screening appointment provides an opportunity to get to know the family, build trust, and screen for underlying medical conditions. Assessment by the MDT provides an opportunity to determine health literacy, health-beliefs and the physical and environmental variables that may act as barriers to change. Outcome measures taken during assessment are described in Table 5.2 and a copy of the clinical assessment form is indexed in Appendix. Careful attention is paid to the communication skills used by the clinical team when meeting the family for the first time. Positive language is used and the family is thanked and encouraged for attending the initial appointment. Given the high levels of stigma and bias experienced by individuals who are obese, positive communication strategies are vital if the family is to become engaged and remain so during the change process (123, 265-270).

5.4.4.5 Participatory Development

The service and accompanying intervention have evolved over time based on the available evidence-base (246, 263, 271) in tandem with qualitative feedback and evaluation from parents and children attending the service. Where possible, behaviour change models and theories are integrated in the daily delivery of the W82GO service so that a balance is reached between the application of theory and real-world practice. Participants are referred

mainly from the local hospital catchment area, which is described as an area of high to extreme disadvantage and deprivation. As such, in many cases, the child's obesity is one of a number of health and social issues faced by the children attending the W82GO service. Therefore, the intervention has been developed to be culturally and socio-economically sensitive (e.g. using a stepped approach to increase fruit and vegetable intake by recommending integration of canned and frozen fruits and vegetables into the diet as a first step towards increasing intake of fresh fruit and vegetables). In order to facilitate differing family situations and dynamics, the service offers both individual and group-based treatment, both inside and outside traditional working hours.

5.4.4.6 Promoting Change via the social network

Based on social cognitive theory, W82GO makes use of social influence to encourage lifestyle change via a supportive network of clinicians, family and friends. The impact of the social network is maximised, by establishing the change process, as a social norm within the group. This is done through weekly goal review, whereby each family reports the goals they have worked on for the previous week and receives encouragement and praise from facilitators and fellow group members. During the games sessions the group is facilitated to work together and to encourage each other (see figure 4.1). In addition, during practical sessions observational learning is promoted such that families observe one-another's changes and methods for managing problems that may arise (e.g. how parents manage adolescents resistant to changes within the home).

5.4.4.7 Family Involvement

Lifestyle change can be usefully understood as an active process involving the entire family. Parents are vital in reducing negative stimuli and increasing positive stimuli within the home and encouraging and reinforcing positive behaviours. Evidence suggests that family-based programmes, where parents take primary responsibility and act as agents for change are likely to be successful for managing childhood obesity (272). Parental and

guardian involvement in W82GO ensures that parents can function as models of positive lifestyle change and can reinforce positive eating and activity behaviour through the use of rewards. Parents are encouraged to think creatively about their use of rewards and to identify non-monetary, non-food rewards for successful goal achievement (e.g. quality family time such as a family outing to a park). Evidence suggests that paediatric obesity programmes incorporating a broader family focus are more likely to be successful (273). Family dynamics can also play an important role, as dual households (where parents are divorced or grandparents play a significant carer role) can lead to a lack of consistency in the support of healthy choices. In addition to parental behaviours that relate directly to eating and physical activity, the service incorporates more general family interventions such as parenting skills and strategies to improve family communication.

Figure 5.1 Group exercise sessions target movement confidence and teamwork in a safe and supportive environment



5.4.4.8 Self-efficacy

Self-efficacy is promoted through the successful achievement of small goals at each stage of the intervention. Self-efficacy is promoted in practical exercise-based and nutrition-related sessions, such as trips to the supermarket to develop participants' skills in making healthy food choices. Situation specific self-efficacy is also promoted e.g. helping parents and children plan how to limit access to treats during festive occasions.

5.4.4.9 Communication

From point of referral to point of discharge, the service aims to utilise optimal communication techniques. All service materials are written in clear and age-appropriate language and where possible a variety of media are used during education and practical sessions to reinforce learning. Throughout contact with the families motivational interviewing techniques are employed in order to facilitate a supportive a non-stigmatising atmosphere (274).

5.4.4.10 Goal Setting

During the screening stage, families are encouraged to identify appropriate long-term objectives and to translate these into specific and achievable short-term goals. This helps to prepare the family for change, based on their individual needs and wants. While engaged in treatment, the families are encouraged to continue with regular goal setting (e.g. through weekly goal review for families attending the group intervention). W82GO incorporates specific training in goal setting, managing barriers to change, and relapse prevention. Goals are based around the positive health behaviours that are promoted in the education and practical sessions, and parents are taught skills needed to implement goals (e.g. steps needed to establish a healthy sleep routine).

Service development: treatment components

5.4.4.11 Physiotherapy

Low levels of physical activity during childhood have been associated with morbidity and mortality in adulthood (275). The physiotherapy component of the service focuses on accurate physical assessment (Table 4.2). Physical activity can benefit children who are obese by increasing their lean body mass, increasing energy expenditure, and improving their metabolic and psychological profiles (276). Independent of any effect on weight, the above changes justify the promotion of physical activity in children. Physiotherapy assessment evaluates global fitness in order to identify structural impairments which may limit time spent in the activity required for weight maintenance (21). In addition, the barriers to physical activity are discussed and can assist with group goal setting around common obstacles. Where physical impairments are identified, a treatment plan is agreed. Treatment incorporates supervised exercise sessions which aim to establish movement and exercise as an enjoyable and rewarding experience for the children involved. Exercise sessions are fun and are tailored to the ability and preferences of the participants. They aim to preserve lean mass, increase aerobic activity and improve motor skill in a safe and secure environment.

Exercise recommendations are specific to the individual child and incorporate both weight bearing and non-weight bearing activities depending on severity of obesity. Successful physical training becomes an important component in the process of enhancing the self-esteem of participants (277). During the programme, the attitudes of the child's parents towards physical activity are also addressed and all members of the family are encouraged to partake in physical activity together (e.g. family outings). In addition to the promotion of physical activity, sedentary pursuits are also discouraged. Television viewing and screen time have been directly related to the degree of obesity in childhood (278). Similarly, given the impact of sleep on child health (279), W82GO manages sleep difficulties as recommended (for example coaching the child and family around establishing a regular bed-time, minimising electronic distractions at night

and optimising the sleep-wake cycle through ambient lighting) (280, 281).

5.4.4.12 Nutrition Component

The increasing prevalence of obesity is likely to be related to changes in nutritional intake, and decreasing children's energy intake may be sufficient to reduce obesity (282). W82GO aims to educate families about healthy eating and balancing energy intake with expenditure in the pursuit of optimal health and growth. Educational and practical sessions aim to increase the family's awareness of healthy eating, age-appropriate portion sizes and swapping high energy-dense foods for more healthy and nutritious options. A main focus is on limiting energy-dense foods with low nutrient value such as sugary drinks (283) to 0-1 servings per week. Similarly, increased intake of fibrous foods which offer greater satiety is encouraged (284), and excessive fat intake which may contribute to weight gain is discouraged (285).

5.4.4.13 Eating behaviour

The national Children's Food Survey (286) indicated that 89% of all meals and snacks eaten by Irish school-children are eaten at home. Therefore while energy intake from restaurants and fast food outlets can be high (287), the home environment has a critical influence on the dietary behaviour and nutrition of children. Parents play a direct role in children's eating patterns through their behaviours, attitudes and feeding styles, and W82GO encourages parents and children to improve their culinary skills in order to prepare healthy meals. In addition, the service promotes behaviours such as: eating together at the table; the preparation of one family meal (rather than a variety of meals for each family member); regular meal-times; the avoidance of using food as a reward for good behaviour; adequate chewing of each mouthful of food and the promotion of adequate hydration to avoid excessive thirst in children (which may often be interpreted as hunger). Finally, W82GO assesses and provides support for children with binge-eating disorders.

5.4.4.14 Behaviour change component

Although education on diet and activity are the core components of obesity treatment, educating children about these two aspects of healthy lifestyle is rarely sufficient to produce the necessary behaviour change. In order to enhance behaviour change, strategies and techniques from the field of behavioural psychology and cognitive behavioural therapy have been applied to the area of obesity (288). W82GO incorporates specific behavioural and cognitive behavioural strategies in order to facilitate behaviour change among participating families. These strategies include: stimulus control; self-monitoring; reinforcement; modelling; self-instructional training and problem solving. For example, structured problem-solving strategies are encouraged whereby parents identify barriers to healthy behaviours and support each other in identifying a range of solutions to these barriers.

W82GO also aims to address the psychosocial issues that are associated with obesity, such as higher rates of psychological difficulties, in particular social difficulties, and lower self-esteem (289, 290). W82GO aims to enhance children's resilience, psychological health, and self-esteem through direct input via information sessions and practical activities for participants. These aim to enhance their self esteem and teach appropriate strategies for managing teasing and bullying (269, 291, 292) as well as indirect intervention, such as teaching strategies to enhance family communication and parenting skills.

Service development: treatment phases

Following assessment, families are invited to attend the intensive treatment phase of W82GO (run two-hourly over 6-weeks for those in group sessions) and thereafter are invited to attend four three-monthly booster sessions (60 minutes) in order to maintain contact and reinforce triggers for positive lifestyle changes. Children are discharged from the service when they maintain a BMI at or below the 95th percentile for more than three months. Onward referral to adult services and transfer arrangements are made for

16 year old adolescents who remain over the 95th centile.

5.5 W82GO development: results

The adoption and implementation of W82GO has been informed by stakeholder feedback and evaluation. Based on the responses of families to a pilot programme, in 2005 the service has evolved to meet the needs and expectations of the majority of families referred. Programme materials such as educational materials, work packs and a website (http://www.w82go.ie) have been developed and are used throughout the service (see Appendix). Seed funding for service development was initially provided by the Temple Street Children's Fund For Health (2005-2007) and in 2007 and 2014 the Health Service Executive awarded a 12-month grant to the service. Unfortunately to date, a formal process evaluation of the W82GO programme has not been possible due to resource limitations. In order to optimise the intervention, future research is warranted to explore programme fidelity, the dose delivered, the dose received and the reach of the intervention (293). In addition further research is warranted to explore the feasibility of implementing W82GO in a community-based setting. Part two of this chapter evaluates the change in obesity observed over 12-months in a series of patients attending the service.

5.6 W82GO development: conclusion

W82GO is an evidence-based theory-informed paediatric obesity service established in line with available guidelines and behaviour change frameworks. In order to deliver the best possible obesity intervention to service-users, it is crucial that on-going monitoring and evaluation of the intervention is completed.

5.7 W82GO development acknowledgements

The W82GO programme would never have been established without the hard work and commitment of the initial team involved in developing the Streetwise Programme (2004-2006). This team included the candidate, Ms.

Anthea Savage, Fiona Boyle and Aisling Shiels. In addition, the service could not have been established without seed funding support from the Children's Fund for Health at Temple Street Children's University Hospital. Thereafter, the W82GO programme was improved and standardised by the team including: the candidate; Aoife Brinkley; Kizzy Moroney; Fiona Ward and John Butler. We thank all of the families involved in W82GO for their feedback and evaluation, which has helped improve the programme. Sincere thanks also to the staff of the Physiotherapy Department who assisted with the implementation of the study, in particular to Lorraine Connolly for help and support with scheduling of patients. The candidate is responsible for the design of the W82GO programme, the design and development of the study website and the design of W82GO information leaflets. The candidate, Aoife Brinkley and Kizzy Moroney are responsible for searching and compiling the evidence underpinning the W82GO programme, the intellectual content of the W82GO participant folder and all presentations used in the programme delivery. Sincere thanks to Grainne Dowdall for her assistance with designing and printing of the W82GO participant folder. The candidate is responsible for writing the above development paper.

CHAPTER 4 PART TWO
W82GO EVALUATION

5.8 W82GO evaluation: background

Systematic reviews of treatment efficacy for childhood obesity report sufficient evidence for well-targeted treatment of children with obesity and meta-analyses indicate that treatment interventions can produce a significant and clinically meaningful reduction in obesity in children and adolescents at 12 months, compared to standard care or self-help (41, 42).

A 12-month reduction in Body Mass Index Standardised Deviation Score (BMI SDS) of 0.14 has been reported in meta-analyses (41) and a reduction in BMI SDS score of 0.25 has been shown to have a significant effect on reducing cardiometabolic risk factors while reductions in BMI SDS of >0.5 improve insulin sensitivity (101, 102, 294). The Temple Street W82GO Healthy Lifestyle Service has been modelled on best practice recommendations as described above and its primary objective is to reduce BMI SDS so that morbidities associated with obesity are reduced (<95th BMI centile)(58, 295).

5.9 W82GO evaluation: aims

The aims of the study were to explore the effect of the W82GO intervention on BMI SDS in children and adolescents between baseline and 12 months, and to estimate the number needed to treat for a clinically significant reduction in BMI SDS of 0.25.

5.10 W82GO evaluation: method

4.10.1 Study design

This is an observational study of consecutive children treated in a hospital-based W82GO Service and a comparable control group.

4.10.2 Participants

All children who commenced the W82GO intervention for management of clinical obesity. Clinical obesity was defined as having a BMI ≥98thpercentile. Participants were referred from the local hospital catchment area, which is described as an area of high to extreme disadvantage and deprivation (296, 297). A group of children on a waiting list served as a control group.

4.10.3 Assessment

The W82GO Service is family-based and is delivered by a multidisciplinary team (MDT) comprised of clinicians from paediatric medicine, physiotherapy, clinical dietetics, psychology and nursing. The MDT assesses children referred to the intervention in order to exclude any medical causes of obesity and to screen for associated comorbidities. Baseline assessment involves the measurement of variables including: anthropometry; physical fitness; nutrition; blood tests; physical activity level; sleep and psychosocial health.

4.10.4 Outcomes

The primary outcome was BMI standard deviation score (BMI SDS). Weight was measured (with participant in socks with no shoes and wearing light clothing) in kilograms to the nearest 0.1 kg using a medical weight scale (SECA, Germany), zeroed and calibrated before each weight. A stadiometer (Harpenden, Cambridge, Md), calibrated in 0.1 cm intervals, was used to determine height. Both height and weight were measured in triplicate and the average value calculated. Body mass index was calculated as the weight in kilograms divided by height in meters squared and BMI SDS and BMI percentiles were calculated using the LMS method (195). As changes in these measures vary considerably according to age, the study group was divided into two age groups - those under 12 years and those between 12 and 16 years. Level of obesity was classified as follows: Class 1 Obesity = BMI SDS 2.00-2.99 and Class 2 Obesity = BMI SDS >3.0.

4.10.5 Intervention

Following assessment, children and parents were offered treatment where the child and their parent/s attended for two phases of the W82GO intervention. Phase one of treatment took place over six sessions and phase two of group treatment was provided at three, six and nine months later. Treatment was offered as a group treatment or as individual treatment based on the choice of the child and parent. The programme incorporated goal setting, self-monitoring and peer support and fostered a supportive atmosphere free of blame or prejudice. In group treatment, phase one was delivered by the MDT over six weekly evening sessions lasting two hours each and in individual treatment, phase one was delivered over six daytime sessions lasting one hour each by the team physiotherapist. The content of the intervention is described in detail in Part A of this chapter. The control group was comprised of 40 consecutive patients who were referred to the service 12-months previously and for whom weight and height measurements had been documented. These children were a consecutive series of children awaiting a clinic appointment.

4.10.6 Statistical analysis

All statistics were performed using SPSS version 20 (IBM Inc. New York). Descriptive statistics were completed and differences between the groups at baseline were calculated with t-tests and ANOVA testing. Changes in anthropometric variables over time were calculated using a general linear model correcting for gender, baseline BMI SDS, age and the time between measurements. Differences between the treatment groups were compared using Bonferroni-adjusted pairwise comparisons. Chi square tests were used to determine the relative number of children who presented with Class 1 and Class 2 Obesity. The 95% confidence intervals for binomial proportions were calculated using the modified Wald method (199). The number needed to treat in order to achieve a 0.25 reduction in BMI SDS over 12-months was estimated by first calculating the proportion of children achieving this reduction in each the treatment and control groups (298). The

proportion (event rate) of children with this reduction in each treatment group was then subtracted from the proportion (event rate) in the control group. The inverse value was calculated to give the NNT for each group (299).

5.11 W82GO evaluation: results

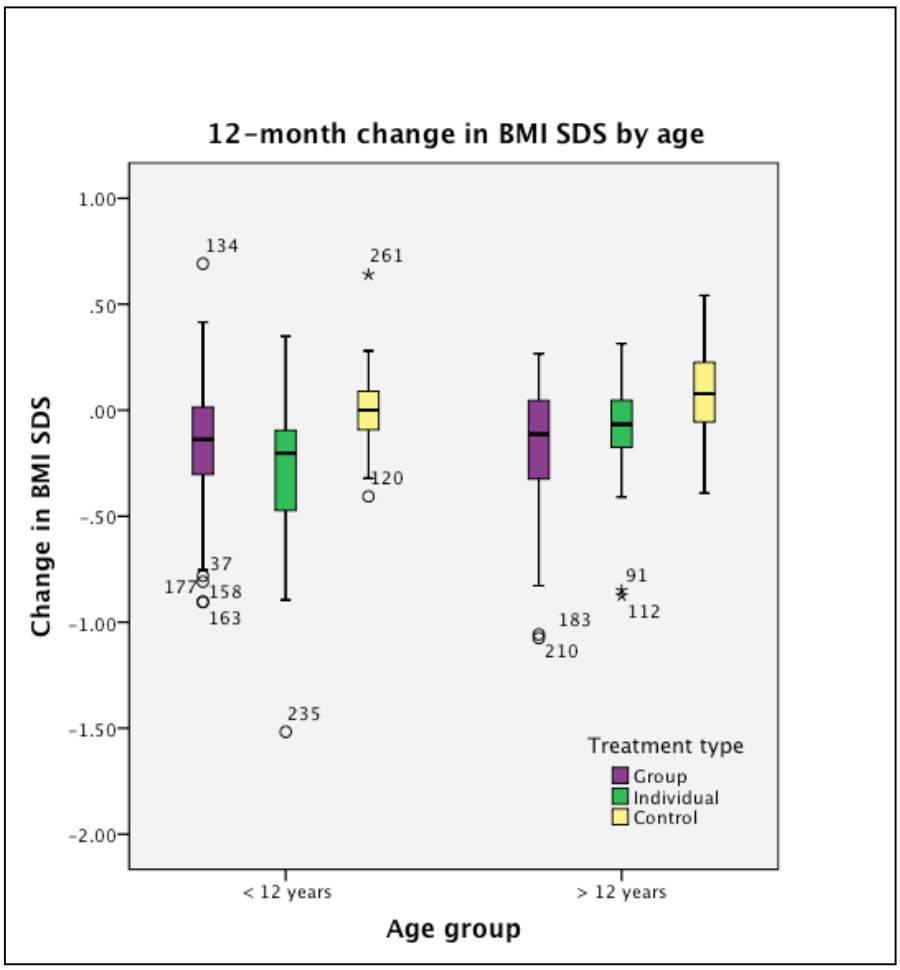
Two hundred and thirty-seven parent-child dyads chose to commence treatment (117 boys, 142 in group treatment) and attended for baseline assessment. In addition there were 40 children in the waiting list control group (15 boys). The baseline characteristics of those being treated and those on the waiting list are described in table 5.3. There were no differences in baseline anthropometry between the treatment or control groups.

Of the 142 children choosing group treatment, 86 were under 12 years. Of the 95 children choosing individual treatment, 56 were under 12 years. Table 5.4 describes the baseline characteristics of the treatment groups by age. Values presented are mean and 95% confidence intervals. Children in group treatment were taller than those in individual treatment (150.9 cm versus 145.0 cm, p=0.04) but no other variables were different at baseline between the treatment groups. In group treatment, 46 children were Class 1 Obese and 96 children were Class 2 Obese. In individual treatment, 37 children were Class 1 Obese and 58 children were Class 2 Obese. In the control group, 10 children were Class 1 Obese and 30 children were Class 2 obese.

4.11.1 Change in BMI SDS over 12 months

Twelve-month data was available for 180 children (88 boys, 112 in group treatment) yielding dropout rates of 21% and 28% in group treatment and individual treatment respectively. Children attending group treatment for which 12-month data was not available were less obese at baseline (mean [95%CI] BMI SDS of 3.03 [2.85, 3.22] versus 3.26 [3.16, 3.36], p=0.04).

Figure 5.2 12-month Change in BMI SDS by age and by treatment group in children receiving W82GO obesity intervention

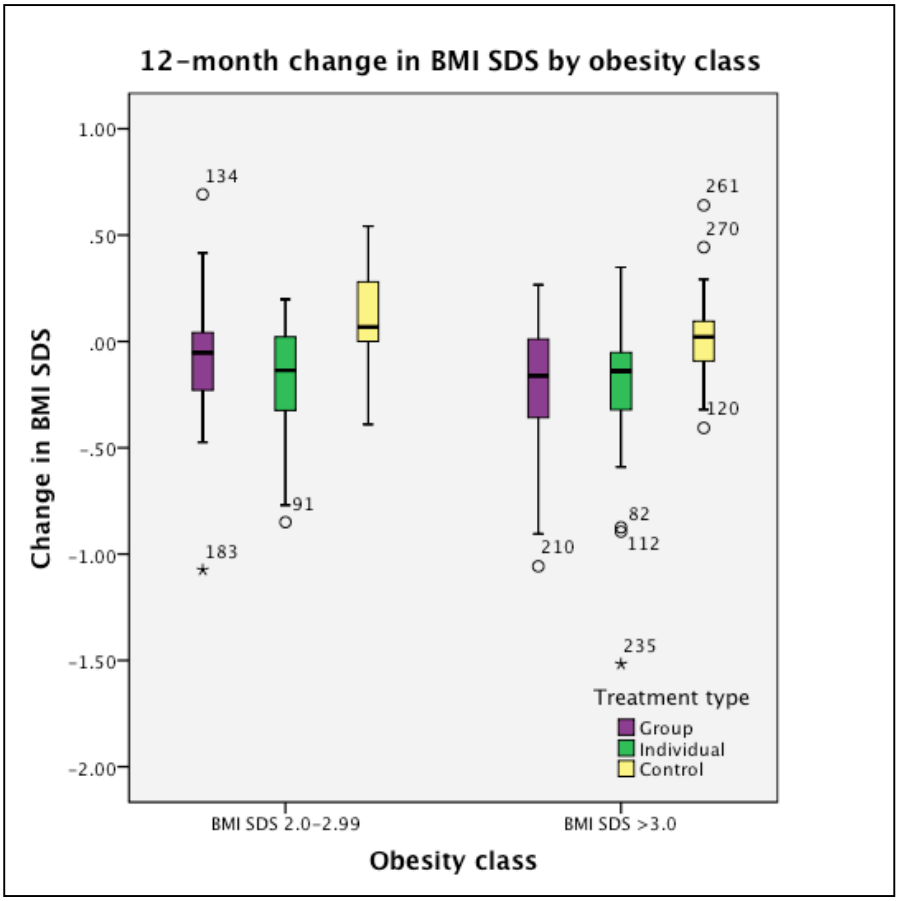


When adjusted for baseline covariates, the overall changes in BMI SDS observed were -0.18 (95% CI -0.23, -0.13) while in the control group BMI SDS increased by 0.05 (95% CI -0.04, 0.14) (F=8.6, p<0.001). The mean difference of group treatment and individual treatment compared to control were -0.23 (95% CI -0.36, -0.11) and -0.23 (95% CI -0.37, -0.10) respectively. Table 5.4 describes the adjusted changes in BMI by age and gender. Figure 5.1 plots the change over time between groups by age category. Younger children had higher reductions in BMI SDS with individual treatment compared to older children (-0.28 (95% CI -0.39, -0.17) versus -0.10 (95% CI -0.20, 0.01), *p*=0.02).

Significant reductions in BMI SDS were observed in girls (under 12 years:

F=6.5, p=0.003 and over 12 years: F=5.9 p=0.004) but not in boys (under 12 years: F=1.6, p=0.2 or over 12 years: F=0.3 p=0.7). BMI SDS was significantly reduced in Class 1 Obesity with individual treatment compared to controls (p=0.048) and in Class 2 Obesity significant reductions were observed in both group treatment (p<0.001) and individual treatment (p=0.008) groups compared to controls (Figure 5.3).

Figure 5.3 12-month Change in BMI SDS by obesity class and treatment group in children receiving W82GO obesity intervention



4.11.2 Number needed to treat

A change in BMI SDS of 0.25 was observed in 32% (95% CI 24%, 42%) of those attending for group treatment, in 31% (95% CI 21%, 43%) attending

for individual treatment and in 13% (95% CI 4%, 26%) of the controls. In group treatment and individual treatment , it is estimated that five and six children respectively would need to be treated in order for one child to achieve this clinically significant change.

5.12 W82GO evaluation: discussion

This study explored the effect of the W82GO intervention on BMI SDS at 12-months as compared to a waiting list control group. At the time of writing, the W82GO intervention was the only treatment available to children who were clinically obese in Ireland. As such, the service had a waiting list of children referred for assessment and treatment. It would be unethical to actively assign children to a no-treatment control group (300) therefore, we used 40 consecutive children for whom a referral height and weight measure was available 12 months prior to being seen in clinic. This study provides data related to childhood obesity treatment. It is limited by the pre-post study design, the small sample size and the lack of randomisation. Nevertheless it reveals the potential for a beneficial effect of W82GO on reducing obesity levels in children and adolescents. We did not include waist circumference as a measure of abdominal obesity as this is challenging to systematically attain due to space limitations and patient embarrassment. In the clinic, private rooms are not always available and at times patients are seen behind curtains in very mall bed spaces. It is not always possible to measure waist circumference adequately and as such, this study did not include the measure. In future we plan to run the clinic in a more suitable space with adequate space for measuring waist circumference in a sensitive manner.

Group treatment and individual treatment were offered to patients in order to facilitate families who did not live within the hospital catchment area and who would be unable to attend the evening sessions of the group treatment due to work or home commitments or travel difficulties. Results of similar obesity interventions have recommended flexibility with mode of delivery in order to optimize patient engagement with treatment (301-304). Given

these restraints, we did not randomise families to group treatment or individual treatment but instead encouraged families to choose the treatment, which would suit their circumstances better. It is important to note, therefore, that there is high risk of bias in the comparison of group treatment against individual treatment, because the groups were self-selecting. Similarly as the control group was comprised of children accepting referral for treatment and given that the group was not randomized there is an additional risk of bias. In this study we did not systematically collect details regarding parental obesity or socioeconomic status (e.g. parental educational level, marital status or parental employment status). As such we could not include these factors as mediators in our analysis. These are limitations given that socioeconomic factors are important determinants in the development of obesity.

When compared to the control group, children in group treatment and individual treatment showed significant reductions in BMI SDS at 12 months which compares favourably to the change of -0.14 (-0.17, -0.12) reported in the 2009 Cochrane systematic review and meta-analyses of childhood obesity treatments (41). Children <12 years had higher reductions in BMI SDS when treated with individual treatment compared to older children who achieved greater reductions with group treatment. This result is supported by previous studies and perhaps reflects the importance of both empowering the parent as the agent of change in younger children (305-308) and the relevance of a peer group for successful treatment in older children (309-311). The overall treatment effect of -0.23 is encouraging as reductions of this level in BMI SDS are associated with improvements to cardiometabolic health in the short-term (100, 215, 312, 313). Similarly, by reducing obesity in childhood and by maintaining such changes into early adulthood, it is plausible that the risk of adult disease associated with childhood obesity could be diminished (30, 56).

Importantly, the treatment benefit was observed in a practice-based setting and as such the study represents the evaluation of an obesity intervention delivered in a 'real-world', setting rather than one delivered to a group of

participants meeting narrow inclusion criteria (314). Similarly, the intervention was developed, embedded and operationalized within the current paediatric health system and thus may have a higher likelihood of being scaled up and sustained, while also narrowing the gap of discrepancy observed between evidence-based research and clinical practice (315-317).

Approximately one third of the children treated did not return for 12-month follow up and although drop-out rates of between 10% and 40% are reported in the literature (41), further work is needed to improve attendance of families at W82GO follow up appointments. Strategies such as SMS texting of appointment-alerts and opt-in appointment times may help to reduce attrition and have been recommended elsewhere (318, 319). This study reported on BMI SDS as the primary outcome and further research is warranted to explore whether the observed benefits are maintained in the longer term and whether the intervention has an impact on other health-related outcomes such as body composition, physical fitness and cardiometabolic health. Similarly, the impact of the intervention on measures of psychosocial health will be important to explore. Data related to self-esteem, self-concept and quality of life are measured at baseline and further study is required to investigate whether the intervention benefits these variables over time.

The second aim of the study was to estimate the number needed to treat in order to achieve a reduction of BMI SDS of 0.25. We observed that 13% of the control group and more than 30% of the treatment groups achieved this reduction. As such, the NNTs for group treatment and individual treatment were estimated at five and six children respectively. Few studies in the literature report estimates of NNT, which hinders comparisons across interventions. However Savoye et al, reported that the NNT required to resolve morbid obesity (BMI to fall below the 95th centile) was 13 for the Bright Bodies intervention when compared to usual care (320). The discrepancy between the NNT estimate in the former and latter studies is likely due to differences in how 'success' was defined. Given the chronic nature of clinical obesity in children, the NNT finding is highly relevant and

has implications for resource allocation and health policy. Further research will be needed to explore the relative cost-effectiveness of providing the W82GO intervention. In addition, ensuring that all children have access to timely treatment is vital and given the developments in the field of health information technology and mobile-health, a pilot study to explore the feasibility of integrating novel technologies into the W82GO service is warranted (321). Similarly, further research to explore the delivery and evaluation of training for community practitioners in the delivery of W82GO is needed. Finally, further evaluation of the W82GO intervention will be required in the form of a randomised controlled trial and the integration of community-based participatory research methods is indicated if W82GO is to be scaled for the wider primary care or community settings (322).

5.13 W82GO evaluation: conclusion

While the evidence described falls short of that provided from a randomised controlled trial, the data suggests that the W82GO intervention was effective in reducing BMI SDS compared to a waiting list control group. Further research is warranted to measure the treatment effect on cardiometabolic outcomes. Data related to the cost-effectiveness of such treatment are also needed.

5.14 W82GO evaluation acknowledgements

The candidate is responsible for the design of the study, data analysis and writing of the paper. The candidate and Dr. Aoife Brinkley were responsible for obtaining financial support for the study from the Children's Fund for Health (PAC11-58). The candidate, Kizzy Moroney, Dr. Aoife Brinkley, John Butler, Dr. Sinéad Murphy and Fiona ward are responsible for the implementation of the study and for data collection. Data collation and data entry were conducted by the candidate and Sinéad Killeen. Thanks to Dr. Tony Fitzgerald of the UCC Department of Epidemiology for his assistance.

Table 5.1 Behavioural change objectives of the W82GO intervention

Behaviour and attitudinal change
1. Increase knowledge and understanding of the benefits of a healthy lifestyle
2. Encourage familial, parental and child attitudes and motivation around change
3. Promote health literacy (e.g. beliefs around behaviour and associated health
4. Improve eating behaviour of the family and child
5. Increase level of physical activity (within school and at home with family and friends)
6. Facilitate personal skills (e.g. self care and cooking skills)
7. Promote the physical and emotional health of the child
8. Improve general parenting skills
9. Increase problem solving skills
10. Improve communication within the family
11. Raise children's awareness of and ability to deal with teasing and bullying
12. Increase children's self esteem
13. Promote quality of life
14. Optimize the sleep routine of the child and family

Table 5.2 Standardised outcome measures used in W82GO clinic assessment

Holistic clinical assessment	
Physical Measures	
Anthropometry	Height, Weight, Waist Circumference
Obesity Classifications	BMI, BMI percentile and BMI SDS
Laboratory Tests	Fasting glucose, insulin, cholesterol, triglycerides; AST, ALT, HbA1c. Measures of insulin sensitivity (197).
Cardiovascular variables	Blood pressure, heart rate, oxygen saturations,
Musculoskeletal Screen	Range of motion, pain, bony alignment, posture, flexibility, strength, gait and balance (21).
Cardiorespiratory fitness	(VO2 peak) Modified Balk treadmill test with heart-rate monitoring and rating of perceived exhaustion (323)
Lifestyle Measures	
Physical Activity Level:	Accelerometry (324, 325) & questionnaire (PAQ) (326)
Quality of Life Level:	PedsQL (327)
Dietary	Standardised nutrition assessment
Sleep	Sleep Disturbances Scale for Children (328)
Psychosocial Measures	
Emotional functioning	Child Behaviour Checklist (329)
Self concept:	The Piers Harris Questionnaire (330)
Eating Habits:	Dutch Eating Behaviour Questionnaire (331, 332).

Table 5.3 Baseline characteristics of participants in the W82GO treament and waiting list control groups

	Treatment Group	*Control Group*
	N=237	N=40
Age (years)	11.0 (10.6, 11.4)	10.7 (9.7, 11.6)
	11.5	11.4
	1.3-16.7	5-15.8
Weight (Kg)	71.1 (67.9, 74.3	69.0 (60.9, 77.2)
	70.6	62.9
	14.0-140.0	29.0-120.0
Height (cm)	149 (146.7, 151.2)	146.8 (141.2, 152.3)
	153.4	147.8
	80.0-179.1	112.9-175.5
BMI	30.8 (30.1, 31.6)	30.7 (29.0, 32.5)
	30.1	29.4
	20.1-50.8	21.8-43.4
BMI SDS	3.23 (3.15, 3.30)	3.24 (3.09, 3.39)
	3.20	3.31
	2.01-5.47	2.21-3.94
BMI Centile	99.8 (99.7, 99.8)	99.8 (99.7, 99.9)
	99.9	99.6
	97.8-100.0	98.7-100.0

Values presented are mean, 95% confidence intervals, median, and minimum and maximum. *p<0.05, **p<0.01. In older children, boys were taller than girls (p<0.001).

Table 5.4 Baseline characteristics of participants in W82GO (group treatment, individual treatment) and control waiting-list

	Group Treatment				***Individual Treatment***				***Control***			
	Boys		Girls		Boys		Girls		Boys		Girls	
	<12	>12	<12	>12	<12	>12	<12	>12	<12	>12	<12	>12
Age (Yrs.)	10.1 9.6, 10.6	13.9 13.3, 14.6	9.1 8.5, 9.7	7.9 6.4, 9.3	7.9 6.8, 8.9	13.6 13.2, 14.0	7.9 6.4, 9.3	14.3 13.5, 15.1	8.6 7.6, 9.6	13.2 12.1, 14.2	8.2 6.8, 9.6	13.2 12.5, 13.9
Weight (Kg.)	61.6 57.6, 65.6	98.6 92.1, 105.1	57.2 52.0, 62.4	94.5 89.3,99.7	50.4 44.3, 56.5	90.2 83.0, 97.4	49.6 38.7, 60.5	85.2 77.4, 92.9	50.5 41.5, 59.6	90.4 66.6, 114	50.5 40.4, 60.6	89.1 78.2, 100
Height (cm.)	146.5 143.2, 149.7	166.0 162.7, 169.4	140.2 135.9, 144.5	161.6 159.6, 163.6	134 127.4, 140.6	163.7 161.1, 166.2	130.2 120.5, 139.9	159.1 156.1, 162.2	134.2 126.9, 141.3	164.5 155.9, 173.2	133.0 1242, 141.9	159.9 155.2, 164.7
BMI (m/kg^2)	28.5 27.4, 29.6	35.7 33.8, 37.7	28.4 27.0, 29.7	36.1 34.4, 37.8	27.0 25.6, 28.3	33.5 31.3, 35.8	27.3 24.8, 29.9	33.6 30.9, 36.3	27.7 24.7, 30.7	32.9 27.4, 38.5	27.7 25.4, 29.9	34.6 31.3, 37.8
BMI SDS	3.17 3.0, 3.35	3.32 3.15, 3.49	3.15 2.97, 3.34	3.28 3.13, 3.44	3.47 3.22, 3.73	3.11 2.92, 3.30	3.24 2.93, 3.5	2.99 2.73, 3.27	3.34 3.05, 3.64	3.11 2.54, 3.67	3.31 3.04, 3.57	3.18 2.84, 3.52
BMI centile	99.8 99.7, 99.9	99.9 99.8, 100.0	99.7 99.5, 99.8	99.8 99.8, 99.9	99.8 99.7, 99.9	99.9 99.8, 99.94	99.8 99.6, 99.9	99.7 99.6, 99.9	99.7 99.5, 99.9	99.9 99.71, 100	99.7 99.2, 100	99.9 99.8, 100

Table 5.5 Change in BMI SDS after 12-months in W82GO treatment and control groups[1]

	Group Treatment				*Individual Treatment*				*Control*			
	Boys		Girls		Boys		Girls		Boys		Girls	
	<12	>12	<12	>12	<12	>12	<12	>12	<12	>12	<12	>12
n	31	14	36	24	23	16	11	10	9	6	12	13
12-month	-0.23	-0.13	-0.18	-0.22	-0.21	-0.14	-0.26	-0.06	-0.07	0.19	0.13	-0.04
Δ in BMI SDS	-0.32, -0.14	-0.28, 0.09	-0.27, -0.08	-0.36, -0.09	-0.31, -0.10	-0.28, -0.08	-0.44, -0.09	-0.28, -0.01	-0.23, 0.09	-0.01, 0.37	-0.04, 0.30	-0.27, 0.20

[1]Values presented are mean and 95% confidence intervals. *p<0.05, **p<0.01. In older children, boys were taller than girls (p<0.001)

6 DEVELOPMENT AND TESTING OF A SMARTPHONE APPLICATION FOR OBESITY MANAGEMENT

6.1 Abstract

Background As technology continues to develop so too do the possibilities for harnessing new innovations to address issues of public health concern. Prevalent yet preventable lifestyle diseases are of particular relevance and could benefit from technologies that use remote sensing to measure risk factors or to deliver interventions using behavioural modification techniques. A growing body of research has employed the Internet and mobile phones in the treatment of obesity. Few studies have focused on the use of mobile-health in children and adolescents specifically, and there is very little data regarding the evidence-based development of smartphone applications used in mobile-health.

Aim The present study aimed to develop a smartphone application (Reactivate) and remote telemedical system for use in adolescent obesity treatment. In addition, we explored the usability (technical effectiveness, efficiency and user satisfaction) of the application, with adolescents classified as obese.

Methods Based on the current literature and on results from an acceptability study a smartphone application and backend software system were developed. Development was conducted in three phases: educational content based on evidence regarding behaviour change was collated, architecture for a backend secure relational database, content management system (CMS) and data management tools were developed and a front-end smartphone application was designed and developed. For usability testing, ten adolescents (12-17 years, 3 girls) who had been treated for obesity (>98th centile for BMI) at the Temple Street Children's University Hospital were recruited. Participants were given eight tasks to complete in order to test the technical effectiveness and the relative user efficiency of the application. In exploration of user satisfaction, each participant completed the standardised Software Usability Measurement Inventory (SUMI) (52), which measures five aspects of user satisfaction: Efficiency, affect, helpfulness, controllability and learnability. Descriptive statistics were used

to explore the mean relative user efficiency and SUMI scores.

Results The Reactivate smartphone application was developed by the candidate and a software developer (Everyfit Inc) for the android platform using an agile scrum iterative process. Current evidence relating to behaviour change theory and human-computer interactions was employed to maximise the usability of the application. During usability testing, adolescents were able to complete all tasks successfully. The mean relative user efficiency scores (mean time taken by a novice user to complete a task compared to the time taken by an expert user) were two to three times that of an expert user. Users responded that they would mainly use the application to monitor their growth over time, for motivation and for goal setting. All users described the application as important for them.

Conclusions: The application is a promising mobile-health tool to be used in adolescent obesity management. A clinical trial is underway to compare the clinical effectiveness of the application as an adolescent obesity management tool as compared to usual care (W82GO).

Keywords: smartphone application, usability testing, human-computer interaction, telemedicine, mHealth, remote treatment, obesity, participatory healthcare.

6.2 Part A: background to development

Obesity management in adolescence, like the treatment of other chronic conditions is challenging and interventions are hampered by the long-term contact required between patients and healthcare providers (333, 334). The challenges experienced by the W82GO service are similar to those reported in the literature for other interventions and include: difficulty in maintaining success after the initial phase of treatment; high rates of attrition; relapse of unhealthy behaviours; the importance of staff training; limited access to treatment due to high demand and the distance needed to travel for treatment (264, 265, 301-303).

Tools and services delivered via online platforms have been suggested as ways to augment assist and support adolescents throughout treatment (335, 336). The use of mobile phone and tablet devices has increased greatly in the past two years and in Ireland in 2014, there were an estimated 2.1 million smartphones in use compared to 1.3 million in 2012 (337). Globally, 968 million mobile phones were sold in 2013 with smartphones making up 54% (146) and the number of all mobile devices sold globally in 2014 (tablets and mobile phones) is projected to reach 2.2 billion (147). The emergence of smartphones that can act as computing handsets which offer voice-calls in tandem with native and Internet-based applications is of potential value to healthcare and public health. The pervasive wireless connection of smartphones provides the opportunity for the communication of multi-media data and their portability releases the user from being attached to a particular location (e.g. a desktop computer). Current smartphones integrate video, audio, recording devices and accelerometry, as well as web-based information services such as geo-location, and social networking which all converge to enhance the user experience. Given the development of mobile technology it is possible to adapt face-to-face obesity interventions for a mobile platform augmenting in-person care and offering secure and effective care remotely (338, 339). Previous work in the area of mobile-health has highlighted the potential benefits of including a remote treatment option in the management of chronic disease (131, 135, 139) and

behaviour change (340). In addition, research in the field of adult weight-management has concluded that mobile-health interventions may be clinically effective (341). The effective design and development of remote and mobile-health interventions is facilitated by iterative development so that optimal functioning for target users is ensured (342-344).

Few data exists regarding the use of mobile-health interventions in adolescents, but studies have reported that SMS texting and image-based interventions are acceptable and perceived as relevant to adolescents who are obese (345, 346). Similarly, although thousands of commercial health and fitness-related mobile applications exist, it is generally unknown whether these applications have been developed in line with best-practice guidelines (164, 338) or with the end user in mind (347). A 2013 review of iPhone and iPad mobile applications for paediatric obesity prevention and treatment reported that over 60% of applications failed to integrate any recommended strategies for childhood weight management (348) as guided by Barlow et al (349). Of 61 applications, only 6 employed strategies to target the multiple lifestyle changes required for effective weight management.

In an effort to augment the W82GO service, the smartphone application has been designed as a remote treatment option for adolescents who are obese. Development of the application included participation by end-users and an acceptability study informed the initial phase of development. The acceptability study was conducted by a colleague of the candidate as part of a master's thesis in cyberpsychology and is described in Appendix V). To summarize, semi-structured interviews and two focus groups with service users were undertaken. These provided qualitative data regarding whether such an application would be considered an acceptable tool for obesity treatment by service-users, and what features the application should include. The main features and issues described by participants included design attributes, the perceived benefits of using an application for treatment, and concerns regarding data protection and privacy.

6.3 Part A: aim of development

The present study aimed to develop a smartphone application and remote telemedical system for use in adolescent obesity treatment. The development process was guided by the current evidence-base and the results of an initial acceptability study.

6.4 Part A: methods of development

Development of the application involved three phases: Developing educational content based on evidence regarding behaviour change, developing architecture for a backend secure relational database, content management system (CMS) and data management tools, and developing and testing a front-end Android-based mobile application. An agile scrum development process was followed (the candidate, the development team - Everyfit Inc.- and the lead developer collaborated in extensive iterative cycles of development).

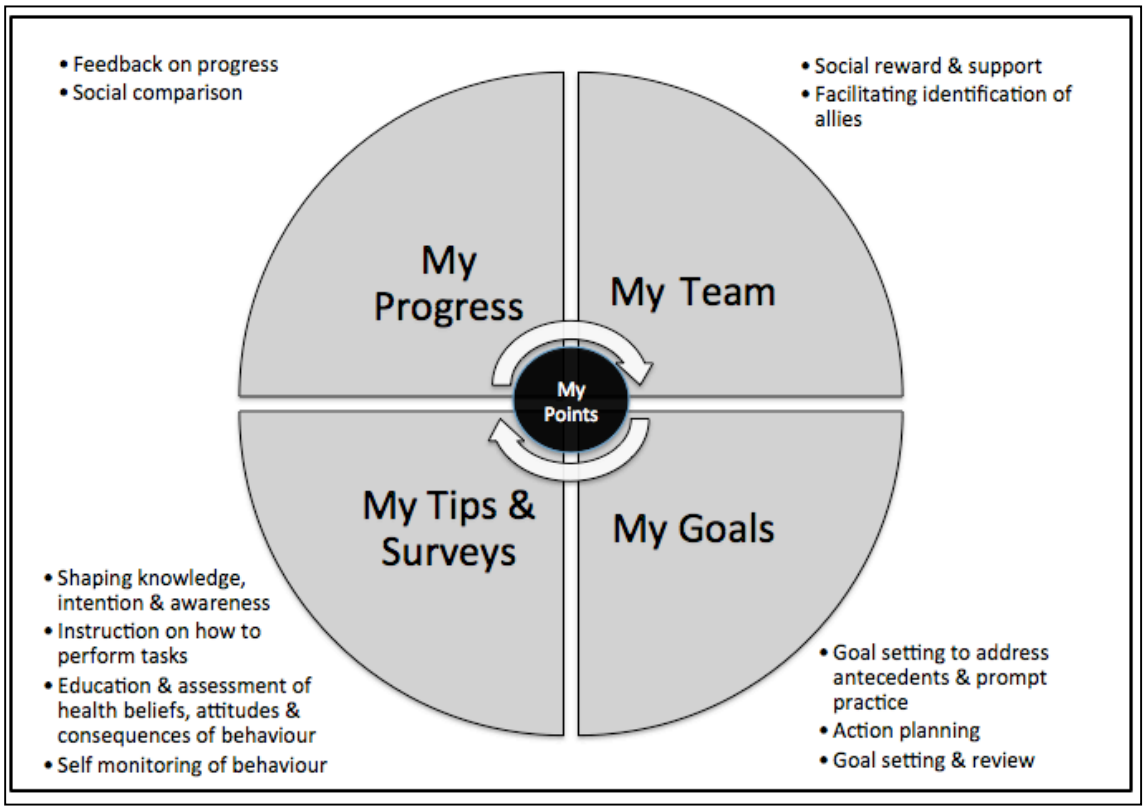
6.4.1 Educational content

The educational information included in the application and the process by which this is delivered to the user is grounded in social cognitive theory, the theory of planned behaviour and the COM-B framework (260, 261, 271). Specifically, the application incorporates behavioural change tools such as self-monitoring, goal setting, a rewards system and peer support (Figure 6.1).

The educational content ("tips") section of the application incorporated information regarding health and development, nutrition, physical activity and sleep as outlined in Chapter 4. It included information on the following topics: Reading food labels; understanding portion sizes; the importance of healthy hydration; understanding sleep, and the importance for healthy growth and development; relaxation techniques; health benefits of physical activity; increasing physical activity; facilitating attentive eating and the importance of social support. The evidence-base for these strategies is

outlined in Table 6.1.

Figure 6.1 Behavioural theory strategies used in mobile application.



Tips were delivered as text-based messages, as image-based messages and as video-based messages. Text-based messages have been shown to promote weight management in adults though the health impact in adolescents is less clear (318). Text-based tips used in the application included the use of emoticons where appropriate. The use of such symbols is reported to assist in accurate interpretation of a message by providing an emotional context and thus enhances computer-mediated communication (319, 350-352). Image-based tips relating to healthy eating and physical activity were used as photo messages and have been found to be helpful to adolescents during weight management (345). Interactive video based messages were provided via a YouTube channel. Video-based education has been observed to promote health-related education, to enhance learning and to facilitate self-regulation (353-355).

The surveys used in Reactive prompted awareness, reflection and self-monitoring (263, 356, 357) by the user regarding daily target behaviours such as increasing physical activity and fibre intake.

6.4.2 Backend system and content management system

Wire-framing using Balsamiq and Adobe Photoshop was undertaken in order to clarify the technical specifications of the application, the screen design the content parameters and the workflow system and application. A MYSQL database was developed on a Groovy/Grails Web framework, which could receive data generated from the CMS and the Android application. During the initial development phase the database was hosted temporarily on a development server and was then ported to the study server.

Each user on the MYSQL database was given a unique identifier, which could map data to a particular phone using the encrypted Android Device identification numbers. All data were encrypted for exchange between the database and the application.

Members of the study team could have access to the CMS and data analytics systems over HTTPS. The CMS was designed to allow the addition and editing of individual participant demographics and response-based data in tandem with customisation and scheduling of content; reflective comments and aggregation of biometric and subjective data captured from the Android device or reported through the CMS. JavaScript charting tool (High charts) was used to visualize data. The CMS incorporated the features described below to complement the behaviour change theory underpinning the application.

6.4.4.1 Customisation and tailoring of surveys and tips

- The clinician could add and edit educational tips in the form of a text-tip, a video-tip or an image-tip. Tips are framed in a positive manner and aim to shape knowledge and awareness and to enhance health literacy by giving information regarding the relationship

between behaviour and health, the costs of action/inaction for adolescents who are obese and the importance of peer and family support for improving health (358, 359). Text-based tips used a motivational interviewing approach and integrated open-ended questions with the option for user reflection (274). Tips were written to address behavioural targets including: Increasing intake of water; reducing intake of sugar-sweetened beverages; increasing fruit, vegetable and fibre intake; reducing fat, sugar and salt intake; consuming appropriate portion sizes; reducing sitting and screen time; improving sleep; increasing daily physical activity to at least 60 mins of moderate-vigorous activity and eating meals as a family without electronic distractions. In addition tips encourage awareness of the obesogenic environment and promoted media literacy. Surveys are used to assess the beliefs and attitudes of the user around health; behaviour and lifestyle change (360). In addition, the survey function is utilized to encourage self-regulation via self-monitoring and self-judgment of health-related behaviours (261). User responses to the tips and surveys are date and time stamped by the CMS.

6.4.4.2 Visualisation of data and trends

- The charting feature of the CMS allows the clinician to view changes in anthropometry and points earned by individual participant or by groups such as age and gender. Data entered into the CMS by the clinician or into the application by the user are date and time stamped. Body mass index, and body mass index standard deviation scores are calculated by the system from height and weight measurements.

6.4.4.3 Facilitating the social network

- The messaging feature was developed to promote the social ties between users (361, 362), and the CMS facilitates the review and moderation of messages sent between users of the application. It includes an alert system to indicate if a user has deemed a message to

be inappropriate or offensive and allows the clinician to disable or enable the messaging feature for individual users.

6.4.4.4 Goal Setting

- The clinician can add to or edit a suite of goals classified into four categories in line with the targeted treatment behaviours (261): "Fuel" goals related to nutritious foods and drinks; "Fun" goals related to physical activity and sedentary pursuits; "Chill" goals related to relaxation, stress management and sleep; and "Change" goals related to environmental and family supports for lifestyle change. The system captures and records all goal-related data as the users utilize the application and sends out daily push notification to prompt reviewing of goals.

6.4.4.5 Rewards and incentives

- A points system can be edited in the CMS in order to allocate points to the user when the use each of the application features. Once the desired points are achieved the system alerts the user and they are entered into a lottery for a prize.

6.4.3 Frontend android application

A native Java mobile application was developed for the Android platform (version 3.0 and later) integrating standard HTML/CSS code, push notifications and following a scrum approach. Development of a native application was chosen over development of a web-based application as evidence suggests that use of a native application increases the probability of continued use (363), and also that a native application can better utilise the capabilities of the hosting devices.

Iterative testing of the application was conducted on the Wi-Fi and 3G network with the final version beta tested on the study server via the 3G and Wi-Fi networks. Beta testing included completion of a usability study (see below). Design assets (logo, icons and screenshots) for the application were

designed using Adobe Illustrator and Adobe Photoshop. The application incorporated the technical features below to complement the behaviour change theory unpinning the application and its use.

6.4.4.6 Rewards and incentives

- A points system can be edited in the CMS in order to allocate points to the user when the use each of the application features. Once the desired points are achieved the system alerts the user and they are entered into a lottery for a prize.

6.4.4.7 My surveys and tips

- User feedback and interactivity are facilitated as the user can view, respond and reflect upon educational tips (text-based, video-based or image-based) and surveys. In addition the user can configure the scheduling of surveys and tips via their personalised settings on the application.

6.4.4.8 My goals

- A core feature of the application brings the user through the process of goal setting in line with Locke and Latham's theory of goal setting and Carver and Scheier's control theory (357, 364). The user is able to choose from a menu of "SMART" goals (364) created by the clinician or instead to create a new goal. Goals are categorised into four categories in line with the targeted treatment behaviours. "Fuel" goals related to nutritious foods and drinks; "Fun" goals related to physical activity and sedentary pursuits; "Chill" goals related to relaxation, stress management and sleep; and "Change" goals related to environmental and family supports for lifestyle change.

  Choosing a goal prompts intention formation since the user is asked to reflect on why this goal is important for them and how difficult it would be to achieve. In addition, the user can set metrics for daily reviewing and monitoring of goals. Up to five goals can be activated each day. Goals are reviewed in the evening and points are earned

depending on the goal achievement rate.

6.4.4.9 My team

- The user can use the text messaging function to promote and maintain social relationships with those using the application (352), thus harnessing peer support for behaviour change (311, 365). The messages are monitored by the clinician using the CMS-hosted tools, but users can also flag inappropriate content and like or dislike messages.

6.4.4.10 My progress

- The user can enter measurement data from home and get feedback by visualising their progress and performance using the charting feature of the application. Charts are displayed for weight, height and BMI standard deviation by week and month, and participants may choose to view their results against those of other users.

6.4.4.11 Personalisation

- The application allows the user to upload a photo of their choice as an identifier or "Avatar". This capability was included as personalisation can increase the importance of a device and creates a stronger attachment between a device and the participant (366, 367).

6.4.4.12 Security

- In the settings section participants are prompted to enable a passcode function so that personal data are protected. Similarly at the device level, there is a prompt to enable the passcode function.

6.5 Part A: results of development

Initial development resulted in the successful creation of a remote mHealth system for use in adolescent obesity treatment. Before finalizing development the front-end mobile application was tested for usability a

group of adolescents who were obese (described in chapter 6 part B).

6.5.1 Backend system and content management system

A user-friendly MYSQL database and web-based content management system (figure 6.3 and 6.4) were developed.

6.5.2 Frontend android application

The screen size of the mobile device was considered when designing icons and logos for the mobile application. Text was used as little as possible and instead colour and symbols were used where possible. Design assets included: the application logo (figure 6.5); icons for each section of the application (figures 6.6-6.9); icons for goal setting (figures 6.10-6.13) and the general arrangement of icons on the screen. Figure 6.14 is a screenshot of the home screen as visualized on a Galaxy Y smartphone (figure 6.15).

6.5.3 Testing

Testing of the application was undertaken using the Samsung Galaxy Y smartphone (GT-55369) with a 2.3.6 Android operating system (Gingerbread). The development team conducted initial beta testing of the application for three weeks with transfer of data from the application to the development server over a Wi-Fi network. Thereafter, the backend database was ported to the study server and a further week of testing was completed over Wi-Fi and 3G networks. Technical issues were catalogued and resolved, and the application was further tested in a usability study (see below section 6B).

Table 6.1 Educational targets addressed in the Reactivate application

Educational topics and strategies
Information on the benefits of a healthy lifestyle(247, 249, 263, 355, 356)
Encourage appropriate portion sizes(269)
Reduce intake of sugar-sweetended drinks(270)
Facilitate attentive/mindful eating(357, 358)
Facilitate cooking skills(359)
Increase fruit and vegetable intake(360)
Increase fibre intake(271)
Reduce saturated fat intake(272, 361)
Limit take-away foods(274)
Increase hydration(362)
Swap refined carbohydrates for those with a lower glycemic index(363)
Remove electronic distractions when eating and sleeping(364-366)
Increase chewing of food and decrease rate of eating(367, 368)
Increase sleep duration(268)
Reduce time spent watching television(265)
Turn off or mute television advertisements(369)
Encourage practice of physical tasks to increase self-efficacy(264)
Increase level of moderate-to-vigorous physical activity to at least 60 minutes per day(370, 371)

Figure 6.2 Screenshot of secure login for clinician content management system for the Reactivate mobile application

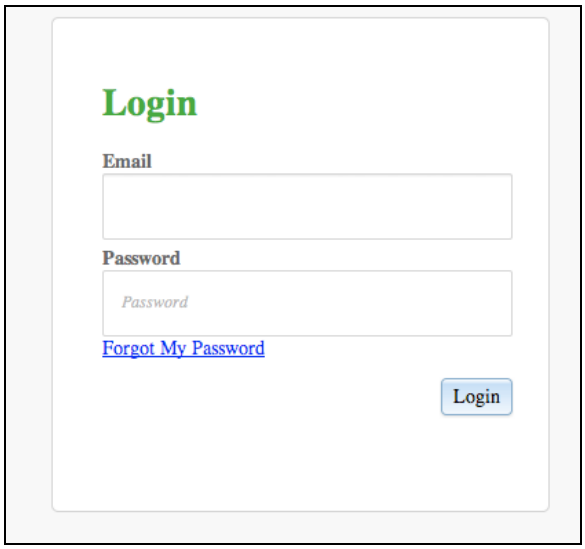


Figure 6.3 Screenshot of clinician content management system for the Reactivate mobile application

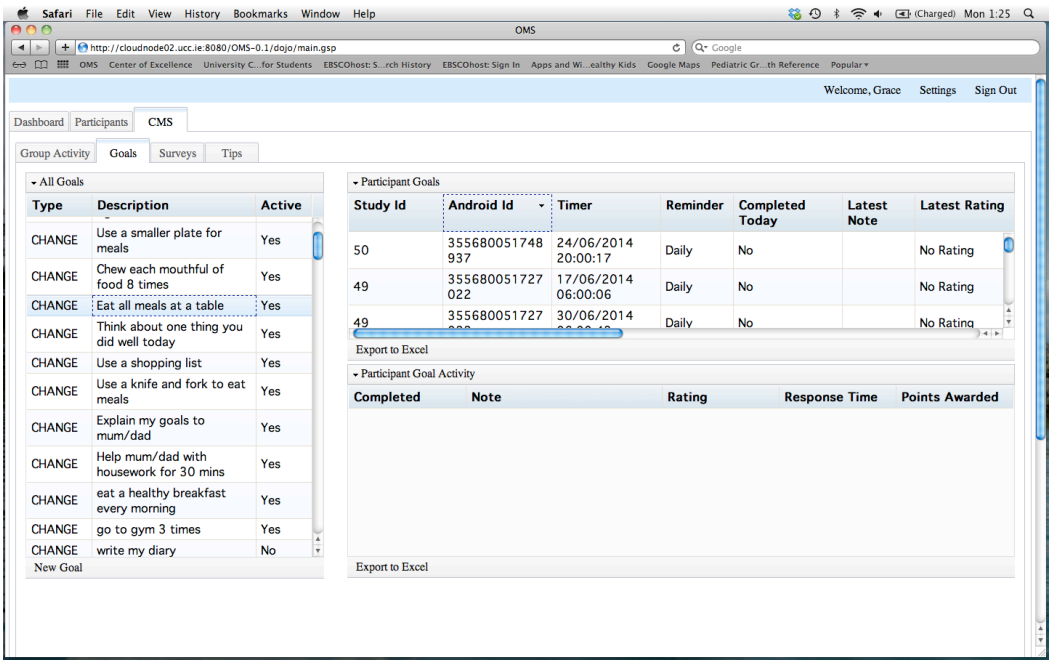


Figure 6.4 Reactivate mobile application icon

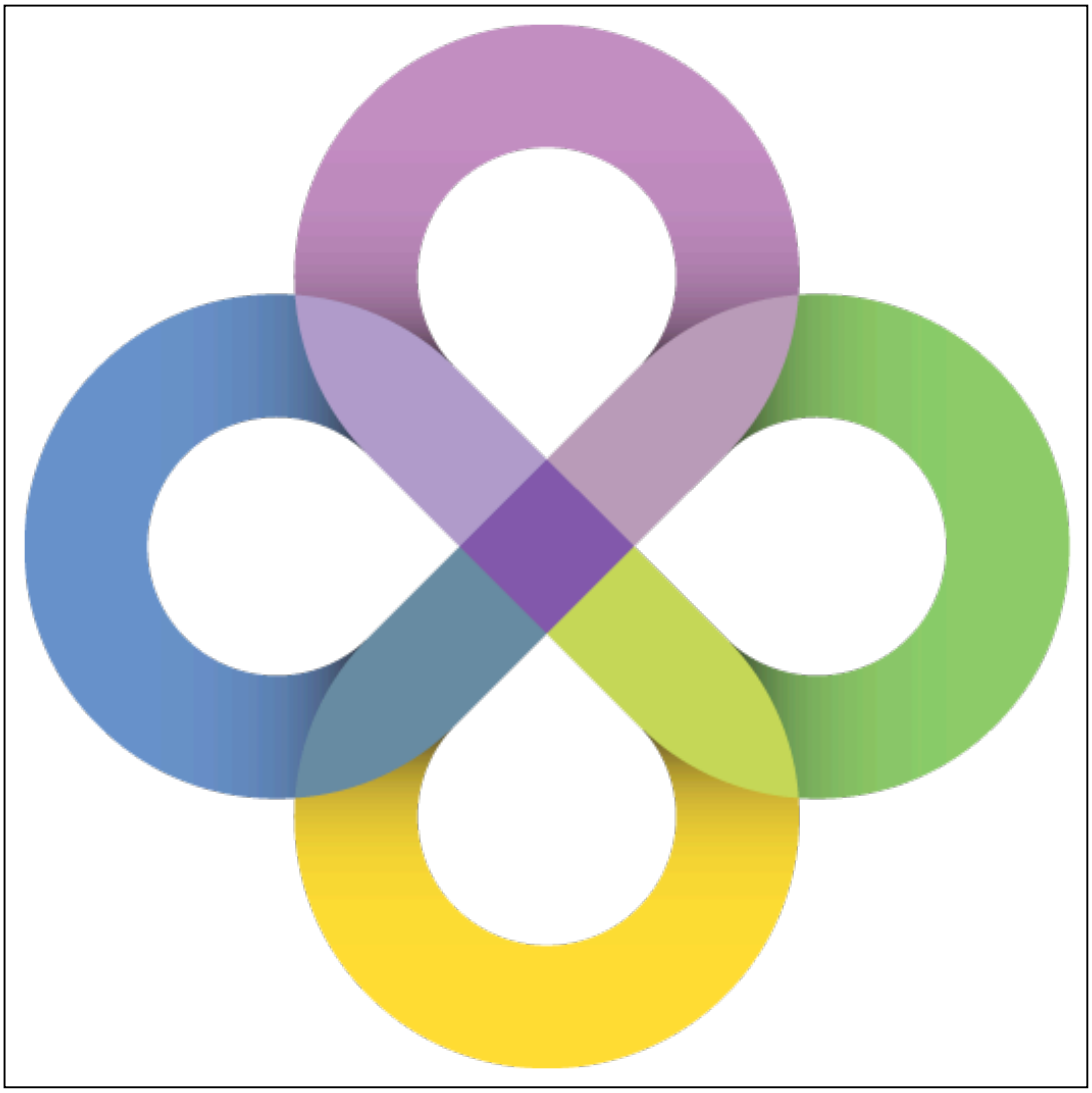


Figure 6.5 Icon for behaviour change strategy: My Progress



Figure 6.6 Icon for behaviour change strategy: My Groups



Figure 6.7 Icon for behaviour change strategy: My Goals



Figure 6.8 Icon for behaviour change strategy: My Tips & Surveys



Figure 6.9 Icon for setting goals related to physical activity



Figure 6.10 Icon for setting goals related to nutrition



Figure 6.11 Icon for setting goals related to sleep and relaxation



Figure 6.12 Icon for setting goals related to environmental change



Figure 6.13 Screenshot of the Reactivate mobile application home screen

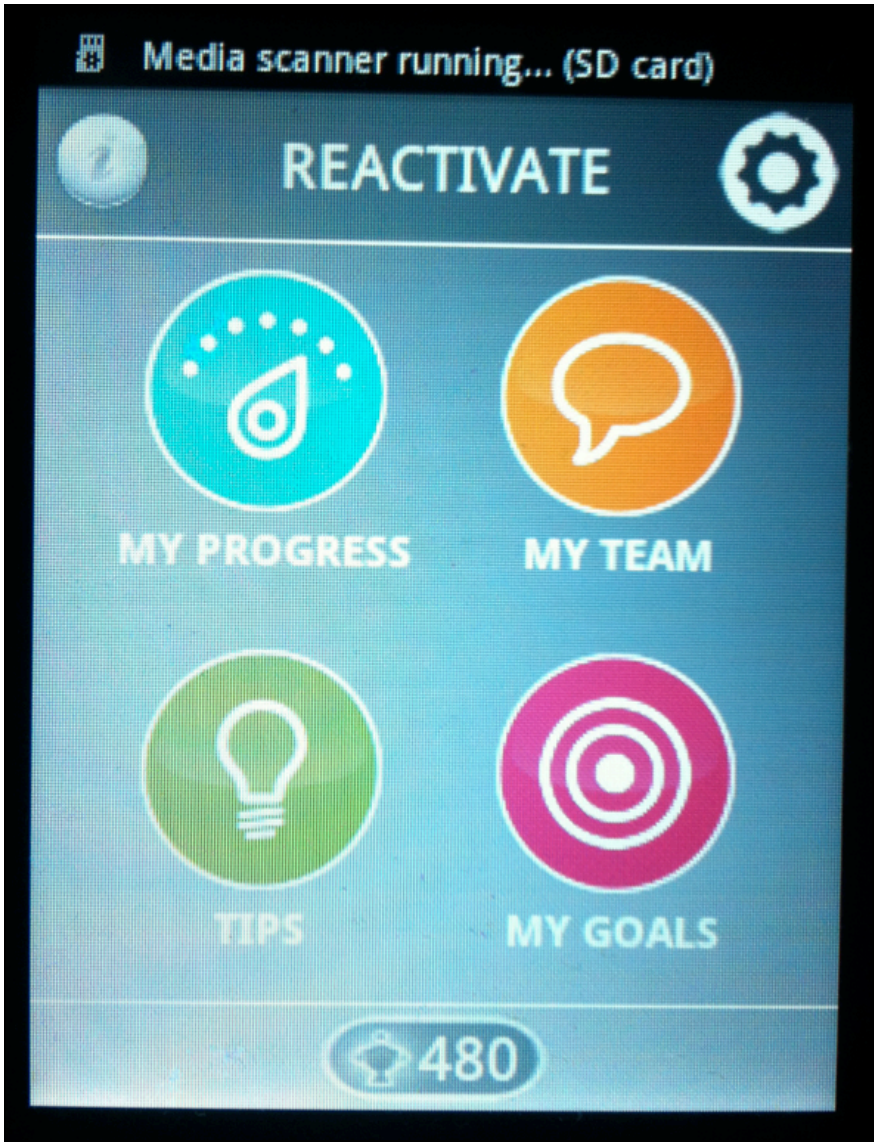


Figure 6.14 Samsung Galaxy Y smartphone



6.6 Part A: discussion

The study developed a smartphone application and mobile-health system for use in the treatment of adolescent obesity. The current evidence base relating to behaviour change theory, health promotion and human computer interactions guided the design and development of the Reactivate application content and technical features.

A number of considerations regarding use of the application arose during development. Firstly, protection of user data is of paramount importance and a passcode feature was integrated into the application to help with this. In tandem it was considered necessary to use a mobile device management system (MDM) during the planned clinical trial. Use of the MDM would facilitate daily monitoring of the users device and allow for all data to be deleted should the device be stolen or lost (168).

Secondly, appropriate moderation of the messaging function was identified as a necessity in order to avoid online bullying or offensive contact between users. It was deemed necessary that parents and adolescents should sign a user agreement contract before using the application in the clinical trial so that parents would take responsibility for the care of the smartphone and their child's use of the application and smartphone.

Future development of the application for the iOS platform will be desirable so that the application can be used across smartphone platforms. Similarly, further development to ensure interoperability with the current health information systems used by the *W82GO* obesity team will be required should the application be rolled out as part of usual care.

6.7 Part A: Conclusions

The application has been designed and developed in line with best practice recommendations for the management of adolescent obesity and is a useful tool for the delivery of a mobile-health intervention.

6.8 Part A: Acknowledgements

The candidate conceived the application, drafted the design assets and wire framing and developed all intellectual content used in the application, its technical features and the behavioural change process used in the application. Prof. Amanda Burls reviewed and contributed to the development specifications of the application. Sincere thanks to Gráinne Dowdall for completion of the acceptability study, which informed the final version of the application. Thanks to Prof. John Morrison (Computer Science, UCC) for assistance with choosing an application development team and thanks to Sombit Mishra from Everyfit Inc. who worked with the candidate to complete the development process.

6.9 Part B: background to usability testing

For adolescents who are identified as being obese, prompt and effective

lifestyle intervention is recommended in order to minimize associated co-morbidities and to prevent further progression of obesity into adulthood. Due to cost and resource limitations, effective obesity interventions can be challenging to deliver to the population of adolescents in need of care. The Temple Street W82GO Healthy Lifestyles Programme, is Ireland's only obesity treatment for children and adolescents at the time of writing (52). Based on recent data, it is estimated that there are around 80,000 children and adolescents who are clinically obese in Ireland (7) and with current clinical service capacity facilitating the treatment of only approximately 150 families per year, it is clear that efforts to scale up treatment are needed.

Given the development of mobile technology it may be possible to adapt face-to-face obesity interventions for a mobile platform and deliver secure and effective care remotely (338, 339) Previous work in the area of mobile-health has highlighted the potential benefits of including a remote treatment option in the management of chronic disease (131, 135, 139). In addition, recent work in adult weight-management has suggested that mobile-health interventions may be effective (340, 341).

The effective design and development of mobile-health interventions is influenced by adequate evaluation of the device interface by the end-user, such that an iterative cycle of development can support optimal functioning of the remote device/intervention (342-344). Little data exists regarding the use of mobile-health interventions in adolescents though studies have reported that SMS texting and image-based interventions are acceptable and perceived as relevant to adolescents who are obese (345, 346).

Although thousands of commercial health and fitness-related mobile applications exist, few developers report whether applications have been developed in line with best practice guidelines (164, 338) or with the end user in mind (347). The user experience with mobile applications varies depending on the smartphone used and users often report difficulty using mobile applications (368) due screen-size, limited processing power, and the incompatibility of applications across devices (369). It is vital that the

end-user is considered throughout the application development process (particularly where the application is to be used by clinical cohorts) and that testing for both technical and clinical effectiveness is completed so that functionality can be optimised.

Recently, electronic-health interventions have been evaluated for usability, and testing has assisted in developing interventions for chronic conditions that are technically effective and acceptable to adolescents (370). The current study aimed to test the usability of the smartphone application with a clinical cohort of adolescents who were obese.

6.10 Part B: methods of usability testing

Usability was defined as the extent to which, the application could be used by a clinical cohort of adolescents who are obese, to achieve specified tasks with technical effectiveness, efficiency and satisfaction. This definition is in line with ISO 9241-11 (52).

6.10.1 Participants

Parent-adolescent dyads that had been attending the W82GO healthy lifestyles programme at Temple Street Children's University Hospital, Dublin, Ireland for at least six months were invited to participate in the study. Adolescents attending the service had a diagnosis of clinical obesity (BMI >98th percentile). The study was approved by the Ethics Committee of Temple Street Children's University Hospital (TSCUH 11-024). Participants were excluded if the adolescent resided in foster care, had a moderate-severe learning disability or if either the adolescent or parent were not proficient in understanding English. Adolescents and their parents who agreed to participate signed age-appropriate consents and assents.

6.10.2 Testing procedure

Usability testing methods proposed by Kushniruk and colleagues and Schneiderman were followed (371, 372). A test plan of three stages was

developed. Stage one sought to test the technical effectiveness of the application, i.e. whether the user could complete a given task or not.

Stage two tested the relative user-efficiency of the application, i.e. the user was timed while he/she undertook standardized tasks in order to examine whether the application was easy to navigate.

Stage three examined user satisfaction with the application. Subsequently, participants representative of the end-users were recruited and eight representative tasks using the application were chosen for testing. Prior to testing, the application was installed on ten Android smartphones (Samsung Galaxy Y). All devices were fully charged and the application was tested to ensure that it had downloaded correctly, was functioning without error and was connected to the Wi-Fi network.

Finally, the manner by which the testing would take place was planned: A usability-testing booklet was developed for participants and for testers in collaboration with the Human Factors Research Group at University College Cork. Usability testing was undertaken at the Vodafone User Experience Centre in Dublin and each adolescent was accompanied by a research assistant/tester. The research assistant, and each adolescent participant, was advised that the aim of testing was to test the application and not the participant and received written and verbal information regarding the testing procedure. Study participants received a brief introduction to the application before usability testing commenced.

6.10.4.1 Technical effectiveness

Participants were given eight tasks to complete in order to test the technical effectiveness of the application. Each task required, or requested, that the participant obtained or inputted specific data that would be used in course of a typical task (table 6.2). The task was completed when the tester indicated that the task goal had been obtained (whether successfully or unsuccessfully) or when the participant requested and received sufficient guidance as to warrant scoring the scenario as a critical error.

A critical error was defined as an error resulting in an incorrect or incomplete outcome. If a participant required assistance in order to achieve a correct output then the task was scored as a critical error and the overall completion rate for the task was affected.

A non-critical error was an error that would not have an impact on the final output of the task but resulted in the task being completed less efficiently. These errors could also be errors of confusion, such as initially selecting the wrong function, using a user-interface control incorrectly such as attempting to edit an un-editable field.

6.10.4.2 Relative user efficiency

Relative user efficiency measured the mean time a user took to complete a task in comparison with an expert user of the application (373). The research assistant timed the user completing each task using a stopwatch in order to test relative user efficiency of the application. Time scores were divided by the time taken by an expert user to complete the task. Throughout the tasks the tester took a written record of any subjective comments made by the adolescent. Upon completion of the tasks subjective opinions were recorded regarding the tasks, time to perform each task, features, and application functionality.

6.10.4.3 User satisfaction

The standardised Software Usability Measurement Inventory (SUMI) (374) was completed by participants at the end of testing to measure five aspects of user satisfaction. SUMI follows the ISO 9241 standard as recognized method of testing user satisfaction. SUMI is a reliable and validated standardised questionnaire where each questionnaire item takes the format of a statement with a fully anchored a 3 point Likert type response, with points named 'Agree', 'Undecided' and 'Disagree'.

Each of the participants responses are scored positively or negatively, depending on the statement, and the scores are summed based on their contribution to each of the five main SUMI factors: *Efficiency* which is the

sense of the degree to which the software enables the task to be completed in a timely, effective and economical fashion; *affect*, the respondents emotional feelings towards the software; *helpfulness*, the perception that the software communicates in a helpful way to assist in the resolution of difficulties; *controllability,* the feeling that the software responds to user inputs in a consistent way; *learnability*, the feeling that it is relatively straightforward to become familiar with the software; and the sixth overall SUMI factor of *user satisfaction* which gives the global score.

A global score of 50 out of 100 is considered to be an average score. Participants completed the SUMI and asked the tester for assistance with wording when necessary. Upon completion of the SUMI, participants were asked to highlight anything they likes about the application or whether they could suggest ways to improve the application.

6.10.3 Statistical analysis

Descriptive statistics of the quantitative data were used to explore the mean relative user efficiency and SUMI scores. Notes and comments recorded during the testing process were transcribed and emergent themes were grouped together.

6.11 Part B: results of usability testing

6.11.1 Participants

Twelve adolescents (12-17 years, 4 girls) who had been treated for obesity were recruited from the obesity clinic. On the day of testing, two families were unable to attend, leaving a total of ten adolescents who participated in testing. The mean (± standard deviation) age of participants were 14.3 (±1.6) years old; mean weight was 84.7 (±55.9) kilograms; mean height was 164 (± 11) cm; mean BMI was 31.1 (±55.9) m/kg^2; and BMI SDS was 2.8 (±0.3).

6.11.2 Technical effectiveness

All tasks were completed successfully and users commented on how the

interface was easy to navigate. Non-critical errors recorded included difficulty in recognising what the application icons represented (5 participants) and that the text was hard to read at times (2 participants).

6.11.3 Relative user efficiency

The time taken by an expert user to complete each task was 5.93 sec. for task 1; 24.37 sec. for task 2; 8.25 sec. for task 3; 17.37 sec. for task 4; 37.50 sec. for task 5; 16.81 sec. for task 6; 20.82 sec. for task 7 and 16.06 sec. for task 8. The mean relative user efficiency scores are detailed in Table 6.3.

6.11.4 User satisfaction

The score results of the SUMI are presented in Table 6.3. All participants rated the application as important (n=9) or extremely important (n=1) for them. Comments made by participants throughout testing of the application included the ease of use (n=2); the benefit of the weight tracking and reward systems (n=9) and the appealing look and feel of the application (n=3). Participants commented that improvements were needed so that the application could run on an iPhone (n=1); that colours could be brighter (n=3) and that text should be larger (n=2).

6.12 Part B: discussion

A representative cohort of obese adolescents who were obese was recruited to test the usability of a smartphone application designed for use in the Temple Street W82GO Healthy Lifestyles Programme. Adolescents who had already commenced treatment were recruited because it was anticipated that they would already have an understanding of the fundamentals of obesity treatment, such as planning and goal setting. In addition, we did not exclude participants based on their level of literacy so that the needs of all users could be taken into account. Overall the results of testing were promising and participants rated the application as important for them and easy to use. Each of the test tasks were completed successfully without critical error indicating that technical effectiveness was achieved.

The relative user efficiency of the application was compared to that of an expert user and the time taken for novice participants to complete tasks was one to three times that of the expert user. As recommended by Bevan (373), measuring the relative user efficiency highlights the potential usability gap between typical users and an expert user and it is anticipated that it often takes normal users two or three times longer to complete a task than an expert. Users were satisfied with the application and reported a number of ways to improve the application further, which were implemented by the developer. A global SUMI score of 64 was promising as an average score is 50 and 68% of software falls within one standard deviation of the mean, i.e. scores between 40 and 60 on the SUMI.

To our knowledge, this is the first study to report on the development and usability testing of a smartphone application to be used as an adjunct to adolescent obesity intervention. Given the popularity of smartphone applications with adolescents and the limited access to evidence-based treatment, we anticipated that a smartphone application would be a useful tool for obesity treatment and the results of this study support this. Strengths of the study include the participation of end-users in an iterative development process and our use of validated methods for testing.

Few studies have been conducted to assess the usability of smartphone application with adolescent patients. One recent study explored the usability of a smartphone application for measuring pain in children with cancer (375). Similar to our findings, participants in the Stinson study (375) commented positively on the aesthetics of the application, on the rewards system and how they would like to use the application again. Testing also revealed important changes to development that were necessary in order for the pain application content to be fully understandable by adolescents and to avoid mistaken navigation away from a chosen page.

With regard to user satisfaction, participants completed a questionnaire and 86% reported that they liked using the pain application while 79% reported that they found it easy to use. The authors concluded that the application

could be used as a tool to assist adolescents in making decisions around pain management.

In a similar study with adult patients with Type 2 diabetes mellitus 25% of participants expressed frustration with using a smartphone application as part of their care due to errors in functioning of the application (376), and a systematic review of applications for diabetes management revealed that the look and feel of the application could impact perceived usefulness (377). Considering our study against the background of previous investigation, it is clear that usability testing is paramount for the optimal design and development of smartphone applications used in clinical cohorts.

Although the test sample for this study might be considered small in number, a minimum of eight participants is recommended in heuristic usability testing (378). We had recruited twelve participants for the study but on the day of testing, two families could not attend and 10 completed the test. Given that testing was undertaken with a group of adolescents attending a single urban hospital for weight management, the results cannot be generalized. Future study is warranted to test the usability of the application with a larger number of participants. In addition, the application should be tested in a cohort of adolescents who are not attending a clinic for weight management, as we do not know whether the users level of motivation for lifestyle change affects their perceptions regarding technical usability.

In addition, as the testing was undertaken in one building using the same Wi-Fi network, we could not ascertain whether the technical effectiveness could be guaranteed when users were dispersed across the 3G network. However, data regarding such limitation will be collected in the on-going randomised trial. In addition, the clinical trial will reveal whether adolescents engage with the application in a 'real-life' scenario over a 12-month period and whether there is dosing effect with regard to use and effect on health outcome.

Finally, we assessed satisfaction of using the application as a whole rather than satisfaction with completing each particular task. Future work to explore each individual component of the application may be warranted.

6.13 Part B: conclusions

Overall the smartphone application performed well in usability testing and results provide support for the usability of the application by end-users. Results of this study guided the final development cycle of the application prior to its use in a randomized controlled trial (NCT01804855). The usability testing of smartphone applications designed to address clinical problems is vital so that the needs of the user can be taken into account such that acceptability and utility is optimized.

6.14 Acknowledgements

The candidate is responsible for conceiving and designing the study, study implementation, data collection, data analysis and writing of the paper. Dr. NoirÍn Curran from the department of applied psychology in UCC contributed to the study design, study implementation and reviewed the paper. Sincere thanks to the adolescents and their parents for choosing to participate in this study and thanks also to the research assistants who took part: Fiona Ward, Robert Rusk and Richard Lambe. Thanks to Dr. Jurek Kirakowski and Dr. Tadeusz Kirakowski for their assistance with the SUMI.

Table 6.2 Tasks used in usability testing of the Reactivate mobile application

Task	Instruction
Task 1	Find and answer the mood survey.
Task 2	Enter your personal settings into the application and save them.
Task 3	Look at the Fizzy drink video in the *Tips* section and choose that you 'like' it. Submit your response.
Task 4	Send a message saying what day it is today and what age you are.
Task 5	Go to the *My Goals* section and pick 2 goals - (one goal from the *Chill* section and one from *Change* section) Make these goals for everyday of the week and set a reminder of 6 pm for each goal.
Task 6	Go to the *My Goals* section and add this new personal goal to the *Fuel* section – I will try a new type of vegetable today (make this goal for everyday of the week and set the reminder for 4 pm)
Task 7	Enter your *height* and *weight* for today, and look at your BMI.
Task 8	Look at your BMI for today and post this on the *Message Board*.

Table 6.3 Relative user efficiency and SUMI scores of the Reactivate mobile application

Parameter	*Mean score (standard deviation)*
RUS Task 1 (seconds)	1.7 (1.3)
RUS Task 2 (seconds)	2.4 (1.4)
RUS Task 3 (seconds)	2.5 (2.1)
RUS Task 4 (seconds)	1.2 (0.8)
RUS Task 5 (seconds)	2.2 (1.3)
RUS Task 6 (seconds)	3.6 (1.7)
RUS Task 7 (seconds)	2.2 (1.2)
RUS Task 8 (seconds)	1.7 (1.3)
SUMI Global	64.4 (5.0)
SUMI Efficiency	60.6 (6.7)
SUMI Affect	67.0 (5.1)
SUMI Helpfulnes	60.8 (8.6)
SUMI Controllability	60.3 (5.1)
SUMI Learnability	60.8 (9.2)

7 mHEALTH INTERVENTION IN ADOLESCENT OBESITY: A MID-POINT REPORT

7.1 Abstract

Background There are few evidence-based mobile health solutions for treating adolescent obesity. The following chapter describes a mid-point report from an on-going randomised controlled clinical trial, which tests the impact of the Reactivate application on health-related outcomes.

Aim To explore whether the effect of the Reactivate mobile application on obesity at 6-months follow up, compared to the W82GO Healthy Lifestyles intervention.

Methods The primary outcome measure was change in BMI SDS at 6-months. Adolescents with a body mass index at or above the 98th percentile (12-17 years) were recruited from the Obesity clinic at Temple Street Children's University Hospital in Dublin, Ireland. Participants received phase one of treatment and were then randomised for phase two to either usual care (UC) or care delivered via the Reactivate application (APP). Intention-to-treat (ITT) and per-protocol (PP) analyses were used to calculate treatment effectiveness and treatment efficacy at 6-months.

Results Forty-six participants (from the target sample size of 134) were randomised to date**.** Follow-up data were available for 19 participants (14 from app). In the ITT analysis, APP participants had a reduction in BMI SDS of -0.11 (-0.19, -0.02) versus -0.07 (-0.17, 0.04) in UC, p=0.6. In PP analysis, APP participants had a statistically significant greater reduction in BMI SDS at 6-months compared to UC (-0.16 [-0.30, -0.02] versus 0.21 [-0.03, 0.46], p=0.02).

Conclusion Data from the mid-point report suggest that there is a statistically insignificant trend for BMI SDS to reduce in adolescents using the Reactivate application compared to those treated with usual W82GO care. Further data is required.

Trial Registration: clinicaltrials.gov NCT01804855

7.2 Background

Data exists regarding the use of technology and mobile applications in a variety of clinical areas including: patient support; smoking cessation; diabetes management and cardiac rehabilitation (379-383). There is however a dearth of data regarding the use of mobile health approaches in the management of adolescent obesity. Chapter five of this thesis described the development and treatment effect of the Temple Street W82GO Healthy Lifestyles programme. In an effort to enhance treatment outcomes, a smartphone application was developed for use in the W82GO programme and was described in Chapter 6. The initial testing of the Reactivate application was promising but in order to ascertain whether the intervention could have an impact on health outcomes, a clinical trial is required. The following chapter describes data from the mid-point report of an on-going randomised controlled clinical trial, which tests the impact of the Reactivate application on health-related outcomes.

7.3 Aim

The primary aim of this study was to assess the preliminary impact of the Reactivate application compared with usual care on BMI SDS over 6-months in adolescents who are obese (12-17 years).

7.4 Methods

7.4.1 Trial design

Randomised non-inferiority clinical trial of 12-months duration where the experimental Reactivate application is compared against usual care in phase two of treatment. Figure 7.1 describes the study design via a study flow diagram.

7.4.2 Participants

Children and adolescents referred to Temple Street Children's University Hospital (TSCUH) for obesity management.

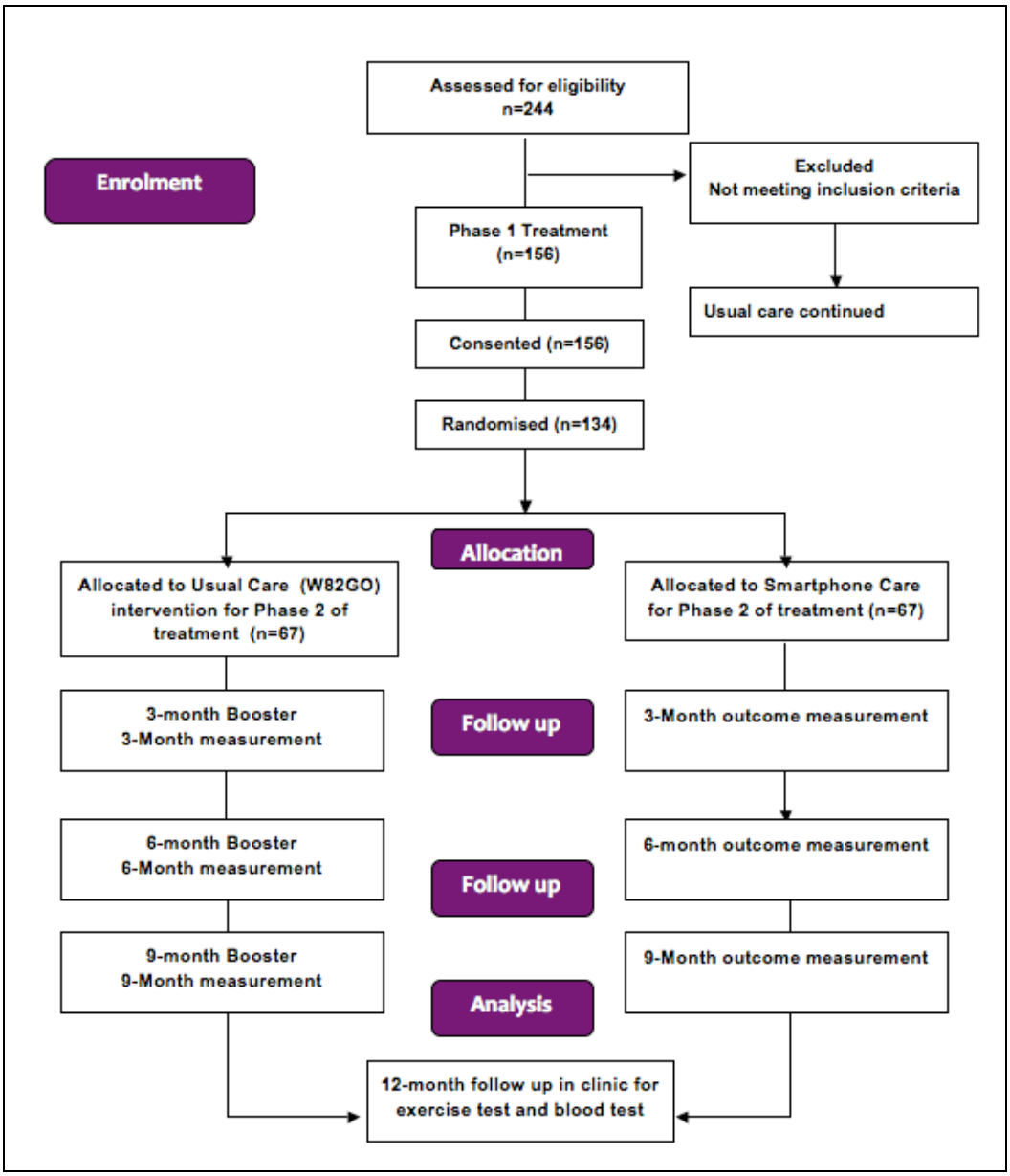
7.4.4.1 Eligibility criteria

- Inclusion criteria: child aged between 12.0 and 17.0 years, child BMI > 98th percentile, first language is English (or fluent in English) and, parent/s willing to participate in the programme with their child and completion of written informed consent and/or assent prior to any study-specific procedures All clinicians based at TSCUH are eligible to refer children to the study.
- Exclusion criteria: severe intellectual difficulties which would limit the child's ability to engage in group activity, obesity secondary to genetic condition, limitations to engaging in physical activity (e.g. active musculoskeletal injury) or use of medication known to effect body weight; limitations to using a smartphone device and known family issues that would affect general compliance and attendance at follow-up visits.

7.4.4.2 Recruitment

Children were recruited from medical clinics and given written information regarding the study. Families wishing to participate in the study were asked to complete consent and age-appropriate parental child assent forms. The motivation and expectations of both adolescents and parents were evaluated during initial assessment and the alternative treatment options were discussed (such as 1:1 versus group treatment in outpatient clinic). It was made clear to parents and their adolescents that by participating in the study they will have a 50:50 chance of being treated in a standard manner or with the Smartphone intervention for phase two of treatment. The study was conducted in agreement with the 'Declaration of Helsinki' and has ethical approval from The Children's University Hospital Ethics Board (11-033).

Figure 7.1: 12-month smartphone trial flow diagram



7.4.3 Randomisation

Eligible adolescents were randomised to either W82GO group (UC) or the experimental group (APP) by the research team using the Sealed Envelope online randomization system with full allocation concealment. Participants were stratified by gender and parental obesity. After randomisation, adolescents were given a study code, which was used to analyse all the data related to that child.

7.4.4 Outcomes

7.4.4.3 Primary outcome measure

The primary outcome was change in BMI SDS at 6-months. Body weight was measured to the nearest 0.1 kg using an electronic scale (SECA, Vogel & Halke, Hamburg, Germany) and height to the nearest of 0.1 cm with a stadiometer (SECA, Vogel & Halke, Hamburg, Germany) in light clothing and without shoes. Measures were taken in triplicate and mean values calculated. BMI was calculated as weight/height squared (kg/m^2) and thereafter BMI SDS was calculated using LMS software (195).

7.4.4.4 Secondary outcome measures

Secondary outcome measurements included: waist circumference; biochemical samples; insulin resistance; blood pressure; body composition; physical activity; physical fitness; health-related quality of life, adverse events and psychosocial health. The following study describes the treatment effect on the primary outcome only.

7.4.5 Intervention

Eligible participants were initially assessed in clinic by a multi-disciplinary team as described in chapter four. Thereafter, patients were offered either group treatment or one-to-one treatment with a member of the clinical team. Prior to the end of phase one of treatment, consented participants were randomised to either UC follow up (four quarterly sessions during the year) or to the Reactivate application only (APP). Phase one was an initial intensive phase and consisted of six weekly sessions for adolescents and their parents. These sessions incorporated educational and practical sessions to increase physical activity; improve nutrition; increase sleep and reduce obesity.

Phase two was a maintenance phase. Upon completion of Phase 1, participants returned with their parents for three 3-monthly booster maintenance sessions over 46 weeks. These sessions aimed to encourage

the family to continue with lifestyle change and to manage barriers to change. In the current study, having completed phase one of treatment, participants were randomized for Phase two to either UC or APP. Full details regarding the W82GO intervention and the Reactivate application are described in chapter four and chapter six.

Participants assigned to the usual care group were given an unlocked Samsung Galaxy Y smartphone and a review appointment was made for three months. Participants assigned to the smartphone group were given a Samsung Galaxy Y smartphone plus the Reactivate application. In addition, a one-gigabyte data plan and free phone calls and texts for 12-months was set up. Participants and their parent/s were then invited to meet the research assistant for a demonstration on how to use the Reactivate application. At this time, the parent took responsibility for the smartphone and both parent and participant signed a user-agreement contract. Thereafter the participant was encouraged to use the application daily, was advised to contact the research assistant on the study phone number should problems be encountered and was given a follow up appointment for three months.

7.4.6 Power calculation for trial

The null hypothesis was that the smartphone intervention would have a positive effect on BMI SDS but that this change will be inferior to usual care. Based on a 0.21 reduction of BMI SDS at 12 months, a standard deviation of 0.24 in the usual care group and a non-inferiority limit of 0.12, the sample size required at 80% power was 50 per group or 100 total. To allow for expected dropout the total number of adolescents to be recruited was 134.

7.4.7 Blinding

Given the nature of the intervention, it was not possible to blind the participants or the care providers. Where staffing to the clinical service allowed, an assessor blind to the participant's treatment allocation measured the primary outcome.

7.4.8 Statistical analysis

All statistical analyses were performed using SPSS (version 20, IBM, New York). The trial was powered for 12-month change, however this study reports preliminary data at 6-month follow up only. As such, we report the change in BMI SDS between the two groups and do not analyse the data for non-inferiority. Descriptive statistics were used to characterise demographic and clinical variables. Chi-square testing was used to compare proportions across groups. An intention-to-treat analysis (ITT) was used to measure change in BMI SDS over time between the two groups. A general linear model (ANCOVA) was used adjusting for baseline age, baseline BMI SDS, gender and any time differences between baseline and follow up measurement. The per-protocol analysis (PP), included participants for whom six-month data was available.

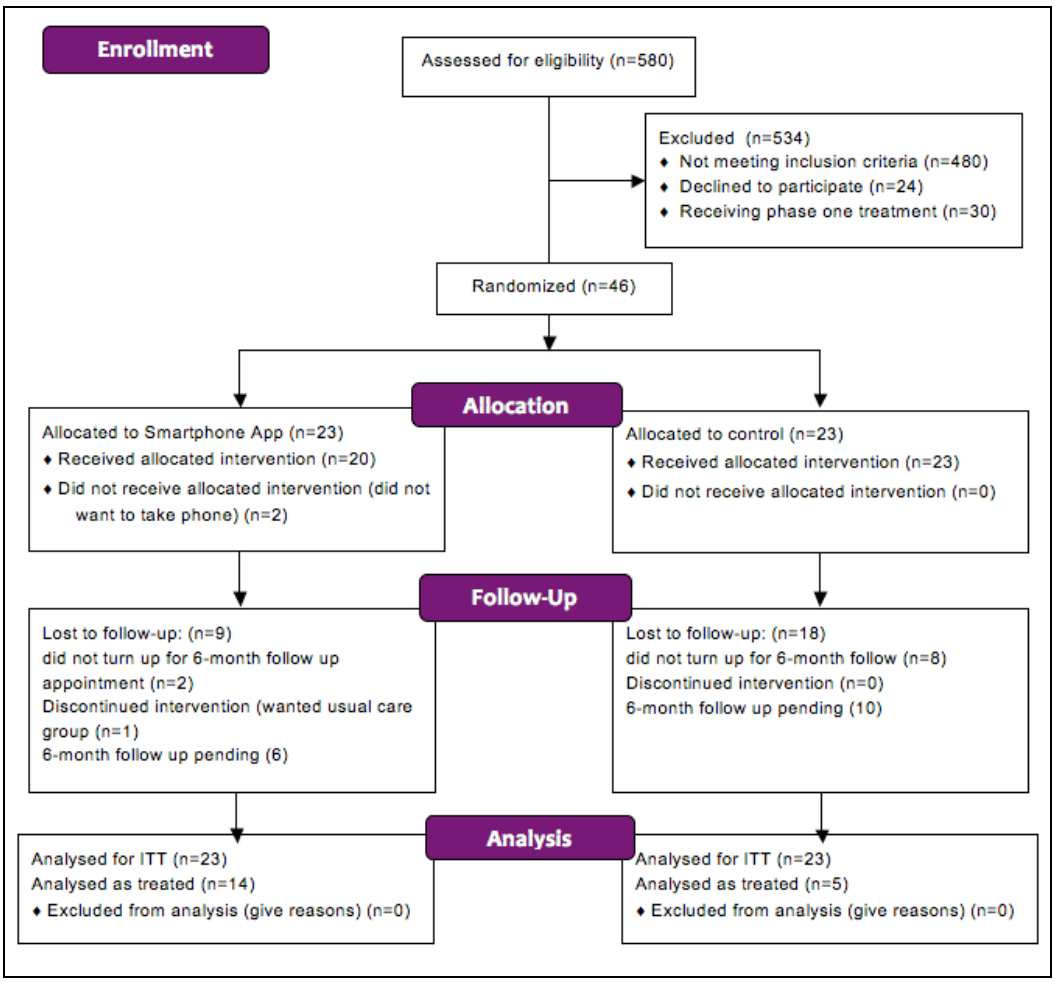
7.5 Results

7.5.1 Participants

Between March 2010 and May 2014, 580 children and adolescents were assessed in the W82GO clinic for weight management and 100 (17%) were eligible for recruitment to the trial. Figure 7.2 Outlines the trial recruitment process via a consort diagram.

As of June 2014 there were 46 adolescents (31 girls) who had completed phase one of treatment (eight chose individual care) and consented to take part in the study. Twenty-three participants were randomised to each study arm (13 girls in smartphone group and 18 in usual care group). There were no differences in the proportion of boys and girls in each treatment group (χ=2.5, p=0.2). Tables 7.1 and 7.2 describe the baseline characteristics of the participants.

Figure 7.2 CONSORT flow diagram of mid-point report from RCT comparing Reactivate smartphone application to W82GO Healthy Lifestyle Intervention



7.5.2 Intervention

Participants assigned to UC received the intervention as per protocol. Forty-four percent of participants in UC and 77% in APP returned at 3-months for the first session in phase two. There were no differences observed between those who returned for follow up versus those who did not with regard to baseline characteristics.

Participants in APP received 294 tips/surveys via the Reactivate application during the 6-month period and there were 1,697 responses received back to the online database from users. Participants using the application earned a mean of 1,107 points (95% CI 628, 1586). APP participants encountered a number of technical problems however; these for the most part involved the

smartphone rather than the application.

Problems included: phone-calls dropping off the network n=4; connection errors when trying to make calls n=3; and freezing of the phone where the phone appeared to be broken (n=2). Additionally, challenges in keeping within the one-gigabyte data limit were experienced by two participants and for a one-week period the server on which the application is hosted was off-line following a period of inclement weather.

7.5.3 Adverse events

During the 6-month trial period, one participant from APP sustained a fractured ankle though this event was not related to the study.

7.5.4 Attrition

Six-month follow up data were available for 19 children (five from UC who were all girls and 14 from APP [7 girls]). As the trial is staggered, participants attend follow-up throughout the year. At the time of writing 16 participants were awaiting a six-moth follow up appointment. No baseline differences were observed for gender or anthropometric measures between those children who attend follow-up and those who did not.

7.5.5. Change in BMI SDS at 6-months

Table 7.3 details the change in BMI SDS (without adjustment for covariates) in the treatment groups. Greater reductions in BMI SDS were observed for APP compared to UC p=0.04. Girls in APP had a greater reduction in BMI SDS at 6-months compared to those in UC p=0.03 (equal variances assumed).

7.5.4.1 Intention to treat analysis

The overall change in BMI SDS at 6-months for all participants with known values was -0.09 (-0.15, -0.02) when all data was considered and adjustments were made for baseline variables (-0.13 [-0.24, -0.02] and -0.04 [-0.16, 0.03] for boys and girls respectively). This change was not

statistically significant (p=0.2). Participants assigned to APP had a greater reduction in BMI SDS at 6-months (-0.11 [-0.19, -0.02] versus -0.07 [-0.17, 0.04], p=0.6).

7.5.4.2 As-treated analysis

Available 6-month data (n=19) was analysed adjusting for baseline variables a reduction in BMI SDS of-0.03 (-0.15, 0.09) was observed at follow up. Greater reductions in BMI SDS were observed for boys compared to girls (-0.19 [-0.39, -0.01] and 0.05 [-0.10, 0.20], p=0.07. Participants assigned to APP had statistically significant greater reduction in BMI SDS at 6-months (-0.16 [-0.30, -0.02] versus 0.21 [-0.03, 0.46], p=0.02) however gender effects complicate this observation.

7.6 Discussion

The study aimed to report the mid-point evaluation on the impact of the Reactivate application compared with usual care on BMI SDS over 6-months in adolescents attending a national obesity management service. Seventeen percent of patients attending the clinic were eligible for recruitment to the study (n=100). It should be noted that in the past three years there have been a greater number of children less than 12 years referred for treatment. As such, recruitment to the trial is on-going and has taken longer than initially anticipated. Recruitment has also been delayed due to an amendment in trial design. When the recruitment process was being piloted the trial design was based on patients being randomised for both phases of treatment. However, over 60% of eligible patients indicated that they did not want treatment delivered via the application only. Instead, families wanted input from the clinical team in a face-to-face setting. This was an important outcome of the pilot process and subsequently the trial design was amended so that phase one was delivered face-to-face. The enrolment refusal rate for the study improved following the pilot process and is currently at 24%. This enrolment refusal rate is lower than the 37% reported in a systematic review (384) of attrition in paediatric intervention

studies and suggests that the amendment of trial design was appropriate. Nevertheless, the generalizability and the validity of the final results will be influenced by self-selection bias and further analysis will be required upon trial completion. It will be important to determine whether there are any systematic differences between those adolescents who agree to take part in the trial versus those who refuse as research suggests that factors including: methods of recruitment; age; race; disease status; family medical history and methods of contact can all affect a family's willingness to participate in intervention trials (385). Similarly it will be important to explore whether there are differences between participating families who attend for follow up and those who drop out of the study. By exploring individual and familial differences we will gain further insight into whether the participating group represents the wider group of adolescents attending our service.

Considering the number of eligible participants seen in clinic and the refusal rate of 24% it is clear that delays in randomising participants should be expected since group sessions can only start when a complement of 12-15 families are available for treatment. Additionally, due to staffing shortages at the time of writing, only one clinician can provide individual treatment. Thus, the number of participants treated is limited to available weekly clinic slots.

To date, just over 17% of eligible participants chose individual treatment for phase one. Reasons for choosing this form of treatment have included: living too far away from the clinic to attend weekly group sessions; parents working in the evening time so unable to attend with participants; or adolescents unwilling to take part in groups. The phase one-treatment option given to patients is a strength of the study and reflects how the trial is integrated into a real-life clinical service. During the trial design phase, it was felt that forcing participants into a treatment (e.g. group) that they would otherwise not have chosen would challenge retention of participants.

As observed in other trials described in chapter two, non-attendance at follow up was high, particularly in UC at 3-months. Karlson et al

systematically reviewed rates and reasons for attrition in 40 paediatric interventions and reported that 20%-38% of children failed to attend for follow up (384). Reasons cited by parents for withdrawal included: being too busy; the project being perceived as too much effort; perceiving the intervention as unnecessary; having to travel too great a distance and having too many appointments. To date, the levels of attrition are higher in UC compared to APP. The reasons for this are currently unknown and there were no anthropometric or demographic differences observed between those who attended for follow up versus those who did not. Further information will be needed regarding the influence of social class on engagement and follow up as demographic details collected to date only include parental separation. As such, information regarding parental occupation, parental educational level and whether the participant attends a designated disadvantaged school will be collected in future. It is possible that simply providing a link between the clinic and the patients increases the likelihood of attending for follow up. Given this result, participants in group treatment who are not partaking in the trial will now be called more regularly in order to maintain regular contact and assist with motivation. In addition, consideration will be given to the future integration of the application (particularly the self-monitoring component) into the standard service so that attrition might be minimised. Perhaps providing all patients with an easy method of monitoring their obesity over time might boost motivation however future study would be required to investigate this further.

The technical problems experienced with the Samsung Galaxy Y handsets and the phone network are worrying. These are a limitation as not all participants are getting the same exposure to treatment via the application. The principal investigator has attempted to limit these challenges via daily monitoring of the mobile device management software. Such monitoring allows the investigator to see when an individual handset is off the network. It does not however, indicate if the participant is having technical difficulties with making calls, texts or transferring data. To address this the investigator

calls the participants fortnightly to ascertain whether they are having technical problems. Similarly, the investigator has negotiated with the phone service provider to classify excess data-use as 'bill-shock' in order to keep costs contained. Collecting data relating to technical difficulties is an essential part of the process-evaluation of mHealth interventions. Clearly in a non-trial setting, users of an mHealth service would download an application to their personal phone. In this case, perhaps fewer technical problems would be anticipated or if they were encountered might be rectified by the user as a matter of urgency. During the trial design process, we felt that it was essential to standardise the phones used in the trial. Such standardisation means that the application can function on a single Android platform using the same handset operating system in an attempt to ensure equal accessibility to the application by participants. Using a single model of handset has drawbacks however. The Samsung Galaxy Y has a small screen (240 x 320 pixels) and two participants have noted that it is excessively small to facilitate frequent use. At the time of writing the handsets were 30 months old and since smartphones are being updated virtually every six-months the model used in the study is considered out-dated by some participants. In addition, nearly 40% of participants already have a new smartphone and as such carry the trial smartphone with them as an additional device. It is currently unclear as to whether having an additional phone influences the time the participant spends using the application and further study will be needed to explore this.

When participants in the smartphone group receive tips and surveys, they have the option to indicate whether they 'like' or 'dislike' the tip. Upon completion of the 12-month trial a qualitative analysis will explore responses and reactions to each educational message and survey sent. This analysis will provide information on the factors influencing whether educational information is perceived as relevant to a user and will guide further development of the application so that tailoring of messages can be enhanced. As the application is currently therapist-assisted, future development will be required to integrate an automated capability. The

qualitative data collected from users in addition to the baseline psychosocial assessment will assist in further tailoring the application to the user and building algorithms to optimise automation. For example the educational content sent to the user could be tailored based on gender, age and whether the adolescent is socially withdrawn. Such tailoring in tandem with automation of the application will allow personalization of the application and potentially improve the effectiveness.

During the six-month trial period, one adverse event was recorded but this was unrelated to the study procedures. As such, no signs of disordered eating, headaches, fatigue or other symptoms of electromagnetic hypersensitivity were noted.

We note in this analysis that the treatment groups were different at baseline as participants in the smartphone group were taller and heavier. However, there were no differences in the groups for BMI SDS (the primary outcome measure). We attempted to reduce selection bias by randomising participants and stratifying the groups with the known confounders of gender and parental obesity. We wanted to test 6-month treatment effectiveness using a pragmatic approach and hence an intention-to-treat analysis was used. We included all participants in this analysis regardless of whether they dropped out of the study or were unavailable for follow up. By including all randomised participants we can be more confident that the groups were comparable and that baseline homogeneity for BMI SDS was not compromised. Overall using an ITT analysis, the six-month treatment difference in BMI SDS between the groups was 0.04 (in favour of APP) but this was not statistically significant. Using a PP analysis we observed a statistically significant treatment difference of -0.37 (-0.66, -0.08) in favour of APP. By using both ITT and PP analyses we attempted to address the observed attrition and to provide information on the effectiveness (via ITT) and the efficacy (via PP) of the treatment.

Our study is limited by the poor attendance rates at follow-up and by the technical difficulties encountered for those allocated to the smartphone arm.

In order to boost attendance at follow-up, an increased number of clinic slots may be required. Nevertheless, the challenges met thus far highlight the difficulty in rigorously testing a complex intervention via a clinical trial conducted in a real-life healthcare setting. Our 12-month data will provide further information regarding the treatment effectiveness of the smartphone application on BMI SDS but also on the secondary outcome measures. In addition, further study will be needed to explore the dose-response relationship throughout treatment. Finally, a qualitative exploration of participant interactivity with the application will be needed to further enhance the application.

The candidate understands that the inability to present full trial data is a limitation to the thesis. However due to the fact that the trial is on-going the candidate felt that presenting data regarding the mid-point evaluation was important and that the data presented in Chapter 7 is appropriate given the data presented in previous chapters. In addition, given the novelty of the intervention, formal presentation of the mid-point analysis is a significant contribution toward the knowledge base accessed by others developing interventions and trials in the area of mHealth and eHealth.

7.7 Conclusion

The mid-point evaluation of the study presents a number of technical challenges to implementing the trial however data suggests that participants using the Reactivate application have lower rates of attrition. Similarly, there is a statistically insignificant trend for BMI SDS to reduce in adolescents using the Reactivate application compared to those treated with usual W82GO care. Further analysis at 12-month follow up will be required to determine clinical effectiveness.

7.8 Acknowledgements

The candidate, Prof. Mike Clarke and Prof. Ivan Perry are responsible for the design of the study. The candidate drafted the study protocol with

suggestions and contribution of all other authors. The candidate was responsible for obtaining financial support for the trial from the Children's Fund for Health (PAC11-58). The candidate, Prof. Perry and Dr. Nuala Murphy were responsible for obtaining financial support from the Health Research Board (HPF2011/54). The candidate, Dr. Sinéad Murphy, Dr. Aoife Brinkley, John Butler and Fiona Ward are responsible for the implementation of the trial and data collection. The candidate was responsible for data analysis and writing of the paper.

Table 7.1: Baseline characteristics of participants in smartphone trial

		Smartphone Group (n=23)	*Usual Care Group (n=23)*	*All Participants (n46)*
Age	Total	14.74 (14.08, 15.39)	14.14 (13.57, 14.70)	14.44 (14.01, 14.86)
(Years)	Boys	15.14 (14.02, 16.27)	14.41 (12.59, 16.22)	14.89 (14.05, 15.74)
	Girls	14.43 (13.55, 15.31)	14.06 (13.42, 14.71)	14.22 (13.72, 14.72)
Weight	Total	97.42[a] (91.55, 103.29)	88.41 (84.64, 92.18)	92.91 (89.30, 96.53)
Kg.	Boys	99.05 (90.22, 107.89)	91.19 (83.99, 98.39)	96.43 (90.31, 102.56)
	Girls	96.16 (87.21, 105.12)	87.63 (82.98, 92.29)	91.21 (86.63, 95.79)
Height	Total	166.45[b] (163.37, 169.53)	162.11 (159.17, 165.05)	164.28 (162.13, 166.42)
cm.	Boys	170.55[c] (165.41, 175.70)	167.10 (158.58, 175.63)	169.40[d] (165.50, 173.30)
	Girls	163.29 (160.01, 166.56)	160.72 (157.61, 163.84)	161.80 159.61, 163.9)
BMI	Total	35.20 (33.10, 37.30)	33.66 (32.19, 35.13)	34.43 (33.17, 35.68)
m/kg^2	Boys	34.09 (31.05, 37.13)	32.72 (29.63, 35.82)	33.63 (31.57, 35.69)
	Girls	36.05 (32.86, 39.25)	33.92 (32.12, 35.72)	33.63 (31.57, 35.69)
BMI	Total	3.18 (3.0, 3.37)	3.07 (3.06, 3.05)	3.13 (3.01, 3.25)
SDS	Boys	3.11 (2.85, 3.37)	3.03 (2.60, 3.46)	3.08 (2.89, 3.27)
	Girls	3.24 (2.95, 3.54)	3.08 (2.90, 3.27)	3.15 (2.99, 3.30)
BMI	Total	99.86 (99.79, 99.93)	99.82 (99.75, 99.90)	99.84 (99.79, 99.89)
Centile	Boys	99.85 (99.75, 99.95)	99.81 (99.57, 100.05)	99.84 (99.75, 99.92)
	Girls	99.87 (99.76, 99.98)	99.83 (99.74, 99.92)	99.84 (99.78, 99.91)

[a, b] Smartphone group taller (p=0.04) and heavier (p=0.01) than usual care. [c] boys in smartphone taller than girls p=0.02. [d] In full group boys taller than girls p=0.001.

Table 7.2: Baseline demographic characteristics of participants in smartphone trial*

	Smartphone Group (n=22)	*Usual Care Group (n=21)*	*All Participants (n43)*
Parental separation	8 (36%)	7 (33%)	15 (35%)
Positive family history of obesity	18 (82%)	13 (62%)	31 (72%)
Parental Obesity	14 (64%)	10 (45%)	24 (56%)
Positive family history of diabetes	14 (64%)	15 (71%)	20 (47%)
Positive family history of cardiovascular disease	10 (45%)	12 (57%)	22 (51%)
Positive family history of hypertension	12 (55%)	14 (67%)	26 (60%)

*Data presented are sample size and percentages.

Table 7.3: 6-month changes in BMI SDS for each treatment group

		All children n=19	*Smartphone Group n=14*	*Usual Care n=5*
6-month Δ BMI SDS	Total	-0.07 (-0.12, -0.01)	-0.14 (-0.27, -0.01)	0.18 (-0.12, 0.47)
	Boys	-0.18 (-0.45, 0.09)	-0.18 (-0.45, 0.09)	-
	Girls	0.01 (-0.15, 0.16)	-0.11 (-0.25, 0.03)	0.18 -0.12, 0.47)

8 DISCUSSION

8.1 Summary of findings

The focus of this Ph.D. was on the important public health topic of childhood obesity. Specifically, the thesis explored management of clinical obesity (BMI >98th centile) in children and investigated the feasibility of integrating mobile technology into the care system. The objectives were to: describe the cardiometabolic burden of obesity in children thereby, highlighting the need for treatment; describe the evidence and effectiveness for lifestyle treatment (including the W82GO intervention); and to develop and test an mHealth tool for use in treatment. Overall the body of work builds on existing evidence related to the management of childhood obesity with family-based lifestyle intervention and describes the potential benefits and challenges posed by introducing a novel intervention into standard care. With regard to a local context the thesis has established and operationalized a paediatric obesity intervention within the healthcare setting and has developed a mobile platform that can be used in other projects and for multiple conditions.

In **Study 1**, a systematic review and meta-analysis of family-based lifestyle treatment of childhood obesity was conducted and meta-analysis revealed that with lifestyle interventions BMI SDS changed significantly by -0.16 (95% CI -0.24, -0.07, p<0.01) at 12-months. The observed treatment effect in **Study 1** is slightly larger than the observed change of -0.14 (-0.17, -0.12) in the 2009 Cochrane review and builds on the scientific knowledge to date regarding the impact of obesity interventions on paediatric health outcomes. The findings of this study highlight inconsistencies in the published literature with regard to the participants and outcomes investigated. To ensure improved decision making by clinicians regarding the most appropriate intervention for a child of a given age and level of obesity, it is

vital that future studies report outcomes based on the developmental stage of the child and their severity of obesity. Similarly, this data will be useful for policy makers when choosing the type of obesity interventions to commission. Both reviews in **Study 1** revealed that few interventions reported on the monitoring of adverse events. The inclusion of adverse events in studies is important as weight loss in growing children can impair linear growth (117, 118), can delay puberty (119) and can reduce bone health (120). Similarly, traditional weight management studies have been reported to stimulate disordered eating (121), negative wellbeing (122) and stigmatisation (123, 124). Additionally, use of mobile devices have been associated with an increased risk of pedestrian injury (386-388); an increased risk of personal theft (389) and could potentially increase the risk of cyber-bullying and online victimisation (390). Clearly, if interventions are to optimised there should be improved reporting regarding adverse events. Overall, the effect size of lifestyle treatments are moderate but should be considered the first line of treatment in a stepped-care approach to manage clinical obesity in childhood.

In **Study 2**, the prevalence of cardiometabolic co-morbidities were estimated in a consecutive series of 267 children living in an urban disadvantaged area. Nearly 50% of the group presented with at least one cardiometabolic co-morbidity and the prevalence of co-morbidities increased as obesity level increased. This study adds to the knowledge base regarding the negative health-effects of obesity in children and highlights the importance of monitoring changes in these variables over time with treatment. As the current mainstay of treatment for such co-morbidities is lifestyle change, this data suggests that nearly 50% of children who are clinically obese may need access to age-appropriate lifestyle treatments in order to prevent further progression of conditions such as hypertension, insulin resistance and hypercholesterolemia. In turn, for children who do not respond to effective lifestyle interventions, additional therapies should be considered to minimize cardiovascular risk.

Study 3 revealed that there was poor agreement between two methods for

measuring body composition in children and adolescents who are obese however changes in body composition using both methods significantly predicted change in metabolic health over time. As body composition is a better index of adiposity, it's use as a measure may be more valuable than BMI alone for identifying children most at risk of cardiometabolic co-morbidity. In practice, considerations such as related cost and expected measurement error should be considered however, measuring body composition as an index of metabolic health may be more appropriate that taking repeated blood tests in some paediatric settings.

In **Study 4**, the evidence-based development and implementation of the W82GO Healthy Lifestyles intervention was described in detail. In a pre-post study the intervention was found to significantly reduce obesity compared to controls and the numbers needed to treat were estimated. This study provides evidence on the feasibility of integrating an obesity service into the existing paediatric healthcare system. The data will aid comparison of obesity interventions based on treatment outcome and are useful for clinicians and policy makers alike.

In **Study 5**, the development and implementation of a mobile application designed as an adjunct to adolescent obesity management was described. This novel study provided important information regarding the development of an mHealth system in line with evidence-based behaviour change theory. In addition the study provides useful data regarding the acceptability and usability of the application with a group of 'end-users'.

In **Study 6**, a randomised clinical trial designed to test the clinical effectiveness of the mobile application was outlined. In addition, the implementation of the trial in a real-world setting was described and the practical challenges of establishing and conducting the clinical trial were outlined. A mid-point report was presented and data suggested that the mobile application might be a promising adjunct for use in the management of adolescent obesity.

Overall, the studies outlined in the preceding chapters highlight that nearly half of children who are obese present co-morbidity and that lifestyle interventions can be effective for obesity management. The studies emphasise the importance of recognising children with obesity, as a heterogeneous group that likely require access to a stepped-care approach. The studies described bring attention to the ethical issues that should be considered including: appropriate trial methodology regarding randomization to no-treatment control groups; the appropriateness of replacing aspects of clinical practice with technology; the potential adverse effects of using mobile phones for healthcare provision, the importance of considering patient needs when attempting to maximise recruitment to clinical trials; the environmental and social impacts of promoting the use of mobile devices for the delivery of wellness and healthcare services and finally the due care that must be given to adequate protection of patient-related data.

The data described suggest that the integration of telemedical approaches into paediatric obesity management is challenging though feasible. In addition data suggested that attrition might be lowered through use of a mobile application and supports previous studies (155, 157, 159, 160). Given the limited access to paediatric obesity interventions in Ireland, integrating telemedical approaches may well be a worthwhile attempt to scale effective treatments. In tandem with appropriate clinical interventions, there is no doubt that preventive measures to curb the development of obesity are urgently required. Such initiatives should be evidence-based, well designed, carefully implemented and regularly monitored in order to optimise their success. Indeed the mobile platform may be particularly suited for the development and delivery of preventive interventions based on behaviour-change models.

8.2 Strengths and Limitations

In **Study 1**, we reviewed the evidence regarding lifestyle interventions in childhood obesity using a systematic approach in line with PRISMA

guidelines. Given the rising rates of morbid obesity, this review was timely. The findings of the review are limited however, as the majority of studies included recruited children who were overweight and obese of various ages. As such, it was not possible to separate studies according to age group or severity of obesity. In addition, the findings are limited as there was wide variation regarding the methodologies used and the quality of trials.

Secondly, we reviewed for the first time the topical subject of mHealth interventions. This study was urgently needed, as there is a significant amount of hype in the industry media and general press regarding the usefulness of mHealth interventions. mHealth approaches were most commonly used to augment a face-to-face treatment and results suggested that a statistically insignificant reduction in obesity was observed.

Study 2 explored the cardiometabolic burden of childhood obesity and was timely as clinical services are grossly unprepared to cope with the myriad of co-morbidities presenting in childhood. Similarly, as Ireland lacks clinical services targeting adolescent health, the finding that many children present with multiple cardiometabolic risks is important. It is likely that adolescents discharged from paediatric services would be placed on long waiting lists while awaiting adult services. Clearly, intermediate care will be required for such children already showing risk of type 2 diabetes and other obesity related co-morbidities. The strengths of this study include the use of standardised techniques and guidelines to define the cardiometabolic burden. Similarly, the analysis of co-morbidity prevalence across classifications of obesity is a strength. Such increases highlight the importance of considering early treatment for children who are obese. Treating severe obesity at an early age is vital as, in adults, those with severe obesity have twice the risk of death from all-cause mortality compared to those with moderate obesity (208). The study was limited by the fact that participants were mainly from the hospital catchment area (an area of severe to extreme disadvantage) and may not be representative of the typical child who is obese in Ireland. Similarly, the study is at risk of self-selection bias as data is drawn from the sample of children who attended for

treatment.

Study 3 examined the use of different methods of estimating body composition. A strength of this study was the use of the Bland-Altman limits of agreement and a criterion method of measuring metabolic health. Data regarding how changes in body composition relate to changes in metabolic function in children are sparse and results of this study add to the evidence published to date. A final strength of this study is that it highlights that BIA should not be considered as a substitute to DXA for the measurement of body composition in a clinical setting. Equally, it is important to note that the two methods should not be used interchangeably in children who are morbidly obese due to within-subject differences.

A limitation of this study was that participants were drawn from a convenience sample, which may have introduced a selection bias. Our group being exclusively obese and the lack of a control group are further issues that limit the findings of Study 4. This study was further limited, as we did not collect standardised information on levels of physical activity and physical fitness. These variables could have influenced body composition (in particular FFM) and indices of insulin sensitivity (237).

In **Study 4**, data described the development, implementation and testing of the W82GO Healthy Lifestyle intervention. A strength of the study was the explicit description of the evidence-based intervention and the involved components. In addition, the experience gained through implementing the intervention within the healthcare setting is of importance if an integrated care pathway for children with obesity is to be realised in Ireland. Refusal rates for treatment, attrition and challenges to long-term engagement emphasize the barriers met when delivering such interventions. For example, the previous experience of children and their parents in the healthcare setting can effect engagement and uptake of treatment. Children with obesity are a vulnerable group who are exposed to levels of stigma and discrimination, which have surpassed racial discrimination (391) and international efforts are underway to develop antidiscrimination legislation

to protect individuals who are obese (392). Research suggests that children who are obese experience weight-based discrimination in the school environment (393) and from healthcare professionals (123). Similarly, those who have experienced weight-based teasing are more prone to disordered eating, lower self-esteem and depression (394) and engagement in treatment can be influenced by the 'ethos' of a particular intervention (301). The research on stigma and discrimination further highlights the sensitivity necessary when working with children with obesity. The study is limited, as we did not collect qualitative data on factors, which might influence engagement in the intervention. In addition, the study is limited, by the pre-post study design, the small sample size and the lack of randomisation. Similarly as the control group was comprised of children accepting referral for treatment and given that the group was not randomized there is a risk of bias. Also, we did not include measurements of body composition (e.g waist circumference) due to resource limitations. Nevertheless, the study described the potential for a beneficial effect of W82GO on reducing obesity levels in children and adolescents and is a valuable contribution to efforts aimed at establishing a fair and equitable healthcare service for children diagnosed as clinically obese.

Study 5 involved the development of the Reactivate mobile application. This study is important, as recently mHealth interventions have been proposed to have the potential to revolutionize healthcare delivery and healthcare practice. This study used the current evidence base relating to behaviour change theory, and health promotion to guide the design and development of the application content and technical features. This study is a valuable contribution to the field of mHealth as highlighted the challenges that can be expected when attempting to implement mobile-based 'solutions' to healthcare problems. Similarly, this study used valid methods from the field of human-computer interactions to test the usability of the application with a group of adolescents who were obese. Reporting on the usability of the application is a valuable contribution to the field of mHealth and overall the results of testing were promising.

During the development of the Reactivate application the protection of patient-related data was addressed. A passcode feature was included to assist with protecting patient data. Similarly use of a mobile device management system facilitates the deleting of personal information should the participant's device be lose or stolen. A further strength of the study is the on-going collection of qualitative data entered into the application by participants. Any response data entered is time and date-stamped and will be used in a qualitative analysis in the future to test whether a dose-response treatment effect exists for those using the application. **Study 5** was limited however, by the small sample used in the usability-testing phase. Similarly, testing was undertaken with a group of adolescents attending a single urban hospital for weight management and as such, the results cannot be generalized.

The limitations of **Study 6** perhaps outweigh the strengths. However it was important for the candidate to provide a mid-way report on data drawn from the clinical trial. A strength of this study is the reporting of the 'real-world' challenges of designing and implementing a randomised clinical trial in paediatric practice in Ireland. In addition, the collection of technical difficulties encountered thus far is an essential as part of the process-evaluation of mHealth interventions. As such, **Study 6** acts as a source of guidance for clinical researchers attempting to conduct similar work. A further strength is that participants had a choice of treatments in phase one of the trial and reflects how the trial is integrated into a real-life clinical service. **Study 6** is limited by the small numbers recruited thus far due to delays in recruitment. Similarly, our findings are limited as we noted the analysis that the treatment groups were different at baseline as participants in the smartphone group were taller and heavier. However, there were no differences in the groups for BMI SDS (the primary outcome measure). Nevertheless, the challenges met thus far highlight the difficulty in rigorously testing a complex intervention via a clinical trial conducted in a real-life healthcare setting. As the study does not blind participants to the allocated intervention there is an extra potential for bias. Our 12-month

data will provide further information regarding the treatment effectiveness of the smartphone application on BMI SDS but also on the secondary outcome measures and the use of both intention to treat and per-protocol analysis will yield important data regarding the effectiveness and efficacy of the intervention.

8.3 Implications of findings

The implications of the findings described in this thesis relate to both research and the practice of clinical paediatrics. In addition, as childhood obesity is a national health priority, the findings may also be useful to public health practitioners and policy makers. Overall results of **Studies 1-3** highlight the challenges encountered when attempting to address the clinical management of obesity. Findings of **Study 1** indicate that lifestyle treatments are effective but treatment effects are modest, and adequate investment will be required in order to facilitate the chronic-care model required for the on-going treatment of clinical obesity in children and adolescents. Additional enhancements to face-to-face treatments may increase the treatment effect. Telemedical services such as video-conferencing and remote monitoring might facilitate such improvements. **Study 2** highlighted the cardiometabolic burden of obesity in children. Clinicians must consider the presence of these co-morbidities carefully and depending on the severity of obesity it will likely be necessary to explore additional treatment options such the use of pharmacological and bariatric interventions.

The results of **Study 3** highlight the difficulty in estimating body composition in children who are morbidly obese but data suggest that monitoring body composition over time might be a useful proxy method for estimating change in insulin sensitivity.

Findings from **Study 4** are in line with other similar interventions with regard to attrition and treatment effect. It should be noted that further work is needed to improve attendance of families at W82GO follow up

appointments. In order to boost attendance at follow-up, an increased number of clinic slots may be required. Strategies such as SMS texting of appointment-alerts and opt-in appointment times may help to reduce attrition and have been recommended elsewhere (318, 319). Appropriate service delivery cannot occur without adequate investment however, and results of this work provide evidence regarding the financial support that will be required if the health service is to deliver effective and equitable care to children who are obese. The results of the numbers need to treat analysis, will guide policy makers on what level of investment will be required in order to a achieve a clinically relevant treatment effect with intervention. Given the chronic nature of clinical obesity in children, this finding is highly relevant and has implications for resource allocation and health policy.

The Reactivate mobile application developed in **Study 5** could be used for the delivery of mHealth interventions in a number of different patient groups. The system is functioning well and can be tailored to meet the need of a variety of patient services. It also meets the aims of the Irish eHealth and connected health strategies. Over the coming years, significant development is expected in these areas and it will be possible to further integrate the application into the information-technology infrastructure of the health system. Future development of the Reactivate application and mHealth platform are warranted and should engage the patient and the wider public in order to design services that are perceived as useful. Internationally demand for telemedical services has increased (395) and a positive impact on training, waiting lists, access to care and financial reimbursement have been reported in the paediatric literature (396-398).

The preliminary findings of **Study 6** indicate that an mHealth intervention might be a useful tool to boost retention in clinical trials and clinical services. As such regardless of the treatment effect, it represents a useful patient education tool. The delays and challenges encountered in the trial are useful to clinical researchers as provide information regarding the expected problems that should be anticipated when conducting similar work. Similarly, these delays highlight funding implications. As the trial was

funded until January 2015 it is likely that additional funding may be required in order to facilitate 12-months of treatment for each participant.

The clinical trial has been delayed due to a number of factors, which should be noted. Firstly, the trial had initially planned to utilise an iPhone application developed by a U.S.-based team. This became untenable as would be hosted outside Ireland by a company who was not signed up to the Safe Harbour Agreement (an E.U directive aimed to protect personal data). Therefore a new application (Reactivate) had to be developed from scratch and we chose the Android platform so that savings in the provision of Android devices (in place of iPhones) could be used to fund development costs.

Secondly, families did not want the application-delivered treatment to replace face-to-face treatment in phase one. As such, every participant recruited to the trial must have phase one treatment before randomisation. This means that for children choosing group treatment in phase one, delays are met by waiting for a sufficient number of families to make up a group (10-15). In turn, delivering the group depends on availability of the. To date, no member of the MDT in TSCUH is employed to exclusively work in the delivery of obesity treatment and as such, other clinical commitments can affect when a group programme can take place. For those choosing individual treatment, there are fewer delays experienced as the candidate delivers this treatment independent of the MDT. Restrictions due to limited clinic space and participant's school commitments are experienced however.

Thirdly, the number of eligible participants has decreased as referrals for the treatment of younger children have increased. Efforts to boost referral of eligible participants were taken by contacting GPs in the Dublin region regarding the trial. A future strategy to boost recruitment might be to target secondary schools by informing school staff about the study and how interested adolescents could partake.

8.4 Implications specific to mHealth interventions

If technology is to be effectively integrated into clinical practice a number of key considerations will need to be addressed. Ensuring that interventions are firmly grounded and supported by evidence is the first step. From the results thus far, there is potential for the Reactivate application to improve patient access to information and education, to enhance the traditional method of treatment used in the hospital and assist with patient adherence to attendance of appointments.

Subsequently, the environment in which the mHealth intervention is deployed should be considered, particularly in terms of technological interoperability. On-going hosting and further development of the application for the iOS platform will hinge on whether the service could realistically be supported in our current health-service. A future cost-effectiveness study will allow further exploration of these issues and whether capacity exists within the health service to scale this research-based initiative into wider clinical practice.

Any interventions delivered to a patient group must ensure data protection and in the world of technology-delivered interventions this is perhaps an even greater challenge. If mHealth interventions are to be used in clinical practice it is essential that guarantees exist regarding the safety of the collected data. Similarly any health-related application needs to be grounded in evidence and in the absence of such data applications should be considered at best as tools for entertainment and at worst as tools to improve the marketing of consumer products and services. Recently a number of technology companies have been implicated in selling personal data and in the field of healthcare such situations could have substantial consequences. This example and other data breeches could be viewed as adverse effects in mHealth trials and future studies should ensure that adequate planning is given to recording and monitoring adverse events related to the intervention itself or to its mode of delivery. The safe delivery of mHealth interventions using tablet, personal digital devices and mobile

phones hinges on the industry regulation regarding the electronic devices themselves, the way in which data is transferred (e.g. via Wi-Fi, Bluetooth or phone networks) and whether having a device increases a user's exposure to harm. For example use of a mobile phone has been associated with an increased risk of poor driving performance (399, 400) (399, 400), an increased risk of driving accident in novice drivers (401), an increased risk of pedestrian injury (386-388); an increased risk of personal theft (389) and could potentially increase the risk of cyber-bullying and online victimisation (390).

Considering the positive and negative attributes of mobile technology, it is currently unknown whether the 'spectres of wireless networks', which surround users of mobile technology and mHealth interventions, confer an overall health benefit or health risk (figure 8.2)

8.5 Recommendations for further research

Based on the studies described herein, future work is required in order to improve the quality of obesity interventions and the reporting of evaluation studies. Studies should endeavour to be consistent in the definition used to classify obesity and statistical analyses should adjust for baseline confounders. Treatment effects should be reported according to severity of obesity. This would aid the reader in drawing conclusions regarding the benefit of treatment for those most severely affected and will allow important comparisons of interventions in high-risk groups who might be considered for surgical rather than lifestyle-based treatment. It is recommended that future studies follow the framework of The Childhood obesity treatment evaluation Outcomes Review (116). Similarly, inclusion of data regarding costs and adverse events will be vital in future studies. Given the inequality gradient associated with obesity. Interventions such as the Bright Bodies programme have shown good results in ethnically diverse groups of children and adolescents who are obese (216, 313, 402-404). As such, future studies should target families of diverse backgrounds and provide clear process evaluation data.

Figure 8.1 The spectres of Wi-Fi



Luis Hernan's 'spectres of Wi-Fi' were photographed using a custom-made scanner, which transforms wireless signal strength transferred by a smartphone to colour light-emitting diodes.

With regard to the W82GO intervention further research is warranted to explore whether the observed benefits are maintained in the longer term and whether the intervention has an impact on other health-related outcomes such as body composition, physical fitness, cardiometabolic health and psychosocial variables. In addition, further research will be needed to explore the relative cost-effectiveness of providing the W82GO intervention.

In addition, further research integrating community-based participatory research methods will be required in order to explore the delivery of the intervention in community settings (322). Such scaling of the intervention would also require additional research on the use of telemedical approaches to treatment. Future development of the mobile application for the iOS platform will be desirable so that the application can be used across smartphone platforms. Similarly, further development to ensure interoperability with the current health information systems used by the obesity service will be required should the application be rolled out as part of usual care. Given the recent focus on personalised healthcare and self-management by funding bodies it is clear that on-going development of the mobile application would align well to national and international eHealth strategies and there is real scope to improve the existing application.

As the clinical trial will continue for a further 12-months valuable data will be explored regarding the impact of the application on health outcomes and qualitative data will aid in improving the application for the delivery of tailored treatment. In summary, a rich dataset has been established and further research to explore whether technology can improve delivery of healthcare in chronic conditions such as obesity will be feasible.

9 CONCLUSION

Results of the studies described in this Ph.D. indicate that family-based lifestyle interventions are a promising form of treatment for paediatric obesity. Lifestyle treatments addressing nutrition, physical activity and behaviour change can significantly reduce obesity at 12-months, but studies exploring the long-term effects of treatment are needed. In addition, meta-analyses will be required to estimate the treatment effects on secondary health-related outcomes. Studies described in the thesis conclude that mHealth interventions may be useful adjuncts to clinical care. At present however, such interventions should not be used to replace clinical care, as there is not enough evidence to support a positive clinical effect. Future studies should explicitly describe adverse events related to the use of mHealth devices. Further, reporting of adverse events is required for future family-based or mHealth lifestyle interventions.

Results of the thesis indicated that children who are obese present with multiple cardiometabolic co-morbidities and it is recommended that children who are clinically obese have access to speciality treatment centres where appropriately trained multi-disciplinary teams can offer a range of treatments. It is likely that pharmacological and bariatric procedures will be needed as adjunctive treatments to lifestyle interventions. Therefore a stepped-care model of treatment in line with other chronic disease management frameworks should be available to Irish children who are obese. As co-morbidities seem to increase as obesity level increases, it is essential that children have timely access to treatment. In addition, children who are overweight and at risk of obesity should have access to appropriate treatment at a community level.

The W82GO intervention is an evidence-based, feasible and clinically effective treatment for children who are obese. It is recommended that the

valuable experience gained in Temple Street Children's University Hospital through the development and delivery of the W82GO intervention, be shared with clinicians and policy makers throughout Ireland. In order to avoid duplication and to build on work completed to date, a hub and spoke model of clinical childhood obesity intervention is recommended whereby a tertiary team at Temple Street act as a training and clinical support hub for satellite teams around Ireland. Future research will be required to explore the effect of W82GO on secondary outcome measures and to estimate the cost effectiveness of the intervention. In addition, further research to adapt the W82GO intervention for a community setting will be needed if the hub and spoke model is to be considered.

The smartphone application was developed in line with the evidence-based and followed best-practice guidelines. The development and integration of the mHealth intervention into clinical practice posed many challenges however, preliminary data suggested that it might be a useful adjunct to the W82GO intervention. Upon completion, on-going research will provide data regarding the cost- and clinical effectiveness of the application.

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APPENDIX I.

DATA COLLECTION TOOL FOR REVIEW OF OBESITY INTERVENTIONS

Data Extraction and Assessment Form – family based treatment of child and adolescent obesity

Study ID:	**Report ID :**	Date form completed:
First author:	Year of study:	Data extractor:
Citation:		

Publication type Journal Article	
Country of origin:	
Funding source of study:	Potential conflict of interest from funding?

Study Characteristics			**Page/**
Type of study	Is Study randomised? Yes ☐ No ☐	Does study have control group? Yes ☐ No ☐	
	What setting is the study conducted in? Details:	*Does the study design meet the criteria for inclusion?* *RCT* *CHILD/TEEN OW OR OB* *FAMILY-BASED TREATMENT* *BMI AS PRIMARY OUTCOME* Yes ☐ No ☐ →**Exclude** Unclear ☐	
Participants	Are participants 18 years or younger? Yes ☐ No ☐	Are participants overweight or obese? Yes ☐ No ☐ Details:	

Types of intervention	*Does the study strategy demonstrate an intent to use a family-based approach?*	☐1. Child & parent/s seen together ☐2. Child & parent/s seen separately ☐3.Siblings invited ☐4. Additional family members involved ☐5. Involves a home-component	
	Does the intervention meet the criteria for inclusion?	Yes ☐No ☐ →**Exclude** Unclear ☐	
Duration of intervention	Start date: / Stop date: / Intervention duration:		
	Is the duration of intervention adequate for inclusion? *(Follow-up must be at least 6 months for all groups)*	Yes ☐ No ☐ →**Exclude** Unclear ☐ Details:	
Types of outcome measures	List primary outcomes *BMI/BMI SDS/BMI centile*		
	List secondary outcomes (*body fat, fitness etc)*		
	Do the outcome measures meet the criteria for inclusion?	Yes ☐ No ☐ →**Exclude** Unclear ☐	
	Are participants defined as having at least one specific social or cultural characteristic?	Yes ☐ No ☐ Unclear ☐	
	Do the participants meet the criteria for inclusion?	Yes ☐No ☐ →**Exclude** Unclear ☐	

Summary of Assessment for Inclusion

Include in review ☐ **Exclude from review** ☐ **NOTES:**

DO NOT PROCEED IF PAPER EXCLUDED FROM REVIEW

APPENDIX II.
SCIENTIFIC ARTICLES PUBLISHED AS PART OF THE PH.D. CANDIDATURE

- O'Malley G, Dowd all G, Clark M, Burls A, Murphy S, Perry I.J. Exploring the Usability of a Smartphone Application for Adolescent Obesity Management. Accepted in JMIR mHealth 2014. 2(2): e29
- O'Malley G, Clarke M, Burls A, Murphy S, Murphy N, Perry IJ. A smartphone intervention for adolescent obesity: study protocol for a randomised controlled non-inferiority trial. Trials. 2014; 15:43.
- O'Malley G, Baker PRA, Francis DP, Perry IJ, Foster C. Incentive-based interventions for increasing physical activity and fitness [10.1002/14651858.CD009598]. 2012. 1

Original Paper

Exploring the Usability of a Mobile App for Adolescent Obesity Management

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Abstract

Background: Obesity is a global epidemic. Behavioral change approaches towards improving nutrition, increasing physical activity level, improving sleep, and reducing sitting time are recommended as best practices in adolescent obesity management. However, access to evidence-based treatment is limited and portable technologies such as mobile apps may provide a useful platform to deliver such lifestyle interventions. No evidence-based validated app exists for obesity intervention; therefore, a novel mobile app (Reactivate) was developed for use in the Temple Street W82GO Healthy Lifestyles Program (W82GO).

Objective: This study aimed to test the usability (technical effectiveness, efficiency, and user satisfaction) of the Reactivate mobile app in obese adolescents.

Methods: Ten adolescents (7 males and 3 females, aged 12-17 years) who had been treated for obesity (>98th percentile for body mass index) at the Temple Street Children's University Hospital were recruited. Participants were given 8 tasks to complete in order to test the technical effectiveness of the app. A research assistant timed the user while completing each task in order to test the relative user efficiency of the app (time-on-task). The tasks fell into 5 categories and required the user to enter personal settings, find and answer surveys, create a message, use the goal setting feature, and enter details regarding their weight and height. In exploration of user satisfaction, each participant completed the standardized software usability measurement inventory (SUMI), which measures 5 aspects of user satisfaction: efficiency, effect, helpfulness, controllability, and learnability. Descriptive statistics were used to explore the mean relative user efficiency and SUMI scores.

Results: Mean age was 14.26 (SD 1.58) years. All adolescents completed each of the tasks successfully. The mean relative user efficiency scores were two to three times that of an expert user. Users responded that they would use Reactivate to monitor their growth over time, for motivation, and for goal setting. All users described Reactivate as an important mobile app.

Conclusions: Our study describes the usability of a mobile app used in adolescent obesity management. Adolescents found Reactivate easy to use and their SUMI results indicated that the app scored high on user satisfaction. Usability testing is an important step towards refining the development of the Reactivate app, which can be used in the treatment of obesity. The study on the clinical efficacy of the Reactivate app is currently underway.

(JMIR mHealth uHealth 2014;2(2):e29) doi:10.2196/mhealth.3262

KEYWORDS

obesity; mobile health; usability testing; adolescent; participatory health care

Introduction

For adolescents who are identified as being obese, prompt and effective lifestyle interventions are required in order to minimize associated comorbidities and to prevent further progression of obesity into adulthood. Due to cost and resource limitations, effective obesity interventions can be challenging to deliver to the adolescent population in need of care. The Temple Street W82GO Healthy Lifestyles Program, (as of May 2014) is Ireland's only obesity treatment for children and adolescents [1]. Based on recent data, it is estimated that there are around 100,000 children and adolescents who are clinically obese in Ireland [2]. With current clinical services facilitating the treatment of approximately 150 families per year, it is clear that efforts to scale up treatment are needed.

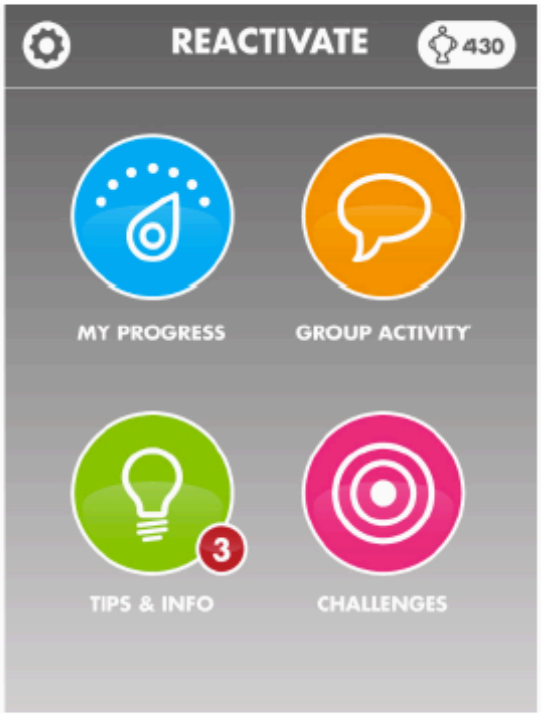
Given the development of mobile technology, it may be possible to adapt face-to-face obesity interventions for a mobile platform and deliver secure and effective care remotely [3,4]. Previous work in the area of mobile health has highlighted the potential benefits of including a remote treatment option in the management of chronic disease [5-7]. In addition, recent work in adult weight management has suggested that mobile health interventions may be effective [8]. The effective design and development of mobile health interventions is influenced by adequate evaluation of the device interface by the end user, such that an iterative cycle of development can support optimal functioning of the remote device/intervention [9]. Little data exists regarding the use of mobile health interventions in adolescents, although studies have reported that short message service (SMS) texting and image-based interventions are acceptable and perceived as relevant to adolescents who are obese [10,11]. In an effort to augment the W82GO service, the Reactivate mobile app has been designed as a remote treatment aid for adolescents who are obese. Development of the Reactivate app included participation by end users and a previous study examining the acceptability of such a mobile app in a separate cohort of parent-child dyads (unpublished data). In short, semi-structured interviews and two focus groups with service users were undertaken to collect qualitative data regarding the necessity of such an app for obesity treatment and the features it must include. The main features and issues described by participants included design attributes, the perceived benefits of using an app for treatment, concerns regarding data protection, and privacy. Design of the Reactivate app was facilitated by contemporarily published evidence-based studies related to obesity interventions and by results from the acceptability study. In brief, the app is underpinned by the social cognitive theory, the theory of planned behavior, and the capability, opportunity, and motivation (COM-B) framework [12-14]. It incorporates behavioral change tools such as self-monitoring, goal setting, a rewards system, and peer support (Figures 1 and 2). Evidence-based tips such as education regarding the importance of sleep for weight management [15] are sent to the user in the form of a text, video, or an image and the user is encouraged to engage in daily goal setting and goal review.

Although thousands of commercial health and fitness-related mobile apps exist, few developers report whether apps have been developed in line with best-practice guidelines [3,16] or with the end user in mind [17]. The user experience with mobile apps varies depending on the type of mobile used and users often report difficulty using mobile apps [18] due to small screen size, limited processing power, and the incompatibility of apps across devices [19]. It is vital that the end user is considered throughout the app development process (particularly where the app is to be used in clinical cohorts) and that testing for both technical and clinical effectiveness is completed so that functionality can be optimized. Recently, electronic health interventions have been evaluated for usability and their testing has assisted in developing interventions for chronic conditions, which are technically effective and acceptable for use in adolescents [20]. The current study aimed to test the usability of the Reactivate mobile app with a clinical cohort of adolescents who were obese.

Figure 1. Schematic of Reactivate behavioral change components.



Figure 2. Screenshot of Reactivate home screen.



Methods

Overview

Usability was defined as the extent to which the app could be used by a clinical cohort of obese adolescents, to achieve specified tasks with technical effectiveness, efficiency, and satisfaction. This definition is in line with the international organization of standardization (ISO) 9241-11 [21].

Participants

Parent-adolescent dyads attending the W82GO healthy lifestyles program at Temple Street Children's University Hospital, Dublin, Ireland for at least six months were invited to participate in the study. Adolescents attending the service had a diagnosis of clinical obesity (body mass index >98th percentile). The study was approved by the ethics committee of Temple Street Children's University Hospital (TSCUH 11-024). Participants were excluded if the adolescent resided in foster care, if they had a moderate to severe learning disability, and/or if either the adolescent or parent were not proficient in understanding English. Adolescents and their parents who agreed to participate signed age-appropriate consents and assents.

Procedure

Usability testing methods proposed by Kushniruk et al and Schneiderman were followed [22,23]. A test plan of three stages was developed. Stage 1, sought to test the technical effectiveness of the app (ie, whether the user could complete a given task or not). Stage 2, tested the relative user efficiency of the app, with the user being timed while he/she undertook standardized tasks in order to examine whether the app was easy to navigate. Stage 3, examined user satisfaction with the app. Subsequently, participants representative of the end users were recruited and 8 representative tasks using the Reactivate app were chosen for testing. Prior to testing, the Reactivate app was installed on 10 Android mobiles (Samsung Galaxy Y). All devices were fully charged and the Reactivate app was tested to ensure that it had downloaded correctly, was functioning without error, and was connected to the WiFi network.

Finally, the manner by which the testing would take place was planned. A usability testing booklet was developed for participants and for testers in collaboration with the human factors research group at the University College Cork – National University of Ireland, in Cork, Ireland. The usability testing was undertaken at the Vodafone user experience center in Dublin and each adolescent was accompanied by a research assistant/tester. The research assistant and each adolescent participant were advised that the aim was to test the app and not the participant. They received written and verbal information regarding the testing procedure, and study participants also received a brief introduction to the app before usability testing commenced.

Technical Effectiveness

Participants were given 8 tasks to complete in order to test the technical effectiveness of the app. Each task required, or requested, that the participant obtained or entered specific data that would be used in a typical task (Table 1). The task was completed when the tester indicated that the task goal had been obtained (whether successfully or unsuccessfully) or when the participant requested and received sufficient guidance to warrant scoring the scenario as a critical error.

A critical error was defined as an error resulting in an incorrect or incomplete outcome. If a participant required assistance in order to achieve a correct output, then the task was scored as a critical error and the overall completion rate for the task was affected. A noncritical error was an error that would not have an impact on the final output of the task but resulted in the task being completed less efficiently. These errors could also be associated with confusion (eg, selecting the wrong function initially, or using a user interface control incorrectly such as attempting to edit an non-editable field).

Table 1. Testing tasks.

Task	Description
Task 1	Find and answer the mood survey.
Task 2	Enter your personal settings into the app and save them.
Task 3	Look at the Fizzy drink video in the *Tips* section and choose that you 'like' it. Submit your response.
Task 4	Send a message saying what day it is today and what age you are.
Task 5	Go to the *My Goals* section and pick 2 goals - (one goal from the *Chill* section and one from *Change* section) Make these goals for everyday of the week and set a reminder of 6 p.m. for each goal.
Task 6	Go to the *My Goals* section and add this new personal goal to the *Fuel* section – I will try a new type of vegetable today (make this goal for everyday of the week and set the reminder for 4 p.m.)
Task 7	Enter your *height* and *weight* for today, and look at your body mass index (BMI).
Task 8	Look at your BMI for today and post this on the *Message Board*.

Relative User Efficiency

Relative user efficiency measured the mean time a user took to complete a task in comparison with an expert user of the app [24]. The research assistant timed the user completing each task using a stopwatch in order to test relative user efficiency of the app. Time scores were divided by the time taken by an expert user to complete the task. Throughout all the tasks, the tester kept a written record of any subjective comments made by the adolescent. Upon completion of the tasks, the subjective comments were categorized based on the tasks, time to perform each task, features, and app functionality.

User Satisfaction

The standardized software usability measurement inventory (SUMI) [1,25] was completed by participants at the end of testing to measure the five aspects of user satisfaction. SUMI follows the ISO 9241, the standard method of testing user satisfaction. SUMI is a reliable and validated standardized questionnaire which uses the agreement type of response. Each questionnaire item takes the format of a statement with a fully anchored 3-point Likert type response, with options being "Agree", "Undecided", and "Disagree". Each item is then scored positively or negatively, depending on the statement, and the scores are summed based on their contribution to each of the five main SUMI factors; efficiency (sense of the degree to which the software enables the task to be completed in a timely, effective, and economical fashion), affect (the respondents emotional feelings towards the software), helpfulness (the perception that the software communicates in a helpful way to assist in the resolution of difficulties), controllability (the feeling that the software responds to user inputs in a consistent way), and learnability (the feeling that it is relatively straightforward to become familiar with the software), and the sixth overall SUMI factor of user satisfaction which gives the global score. A global score of 50 out of 100 is considered to be an average score. Participants completed the SUMI and asked the tester for assistance with wording when necessary. Upon completion of the SUMI, participants were asked to highlight anything they liked about the app or give their suggestions on improving the app. Descriptive statistics of the quantitative data were used to explore the mean relative user efficiency and SUMI scores. Notes and comments recorded during the testing process were also transcribed and emergent themes were grouped together.

Results

Participant Characteristics

Twelve adolescents (8 boys and 4 girls, aged between 12 and 17 years) who had been treated for obesity were recruited from the obesity clinic. On the day of testing, two families were unable to attend. Hence, a total of 10 adolescents participated in the study. The mean age of participants was 14.3 (SD 1.6) years old; mean weight was 84.7 (SD 55.9) kilograms; mean height was 164 (SD 11) cm; mean body mass index (BMI) was 31.1 (SD 55.9) m/kg^2; and BMI standard deviation (SD) score was 2.8 (SD 0.3).

Technical Effectiveness

All tasks were completed successfully and users commented on how easy the interface was to navigate. Noncritical errors recorded included difficulty in recognizing what the app icons represented (5 participants) and difficulty with reading the text on the app at times (2 participants).

Relative User Efficiency

The time taken by an expert user to complete each task was 5.93 seconds for task 1; 24.37 seconds for task 2; 8.25 seconds for task 3; 17.37 seconds for task 4; 37.50 seconds for task 5; 16.81 seconds for task 6; 20.82 seconds for task 7 and 16.06 seconds for task 8. The mean relative user efficiency scores (RUS) are detailed in Table 2.

User Satisfaction

The score results of the SUMI are presented in Table 2. All participants rated the app as being important (n=9) or extremely important (n=1) for them. Comments made by participants throughout testing of the app included the ease of use (n=2); the benefit of the weight tracking and reward systems (n=9), and the appealing look and feel of the app (n=3). Participants commented that improvements were needed so that the app could run on an iPhone (n=1); that the colors could be brighter (n=3), and that the text could be larger (n=2).

Table 2. Relative user efficiency and SUMI scores.

Characteristic	Mean (SD)
RUS Task 1 (second)	1.7 (1.3)
RUS Task 2 (second)	2.4 (1.4)
RUS Task 3 (second)	2.5 (2.1)
RUS Task 4 (second)	1.2 (0.8)
RUS Task 5 (second)	2.2 (1.3)
RUS Task 6 (second)	3.6 (1.7)
RUS Task 7 (second)	2.2 (1.2)
RUS Task 8 (second)	1.7 (1.3)
SUMI Global	64.40 (4.99)
SUMI Efficiency	60.60 (6.70)
SUMI Affect	67.00 (5.06)
SUMI Helpfulness	60.80 (8.63)
SUMI Controllability	60.30 (5.06)
SUMI Learnability	60.80 (9.21)

Discussion

Principal Findings

A representative cohort of adolescents who were obese was recruited to test the usability of a mobile app designed for use in the Temple Street W82GO Healthy Lifestyles Program. Adolescents who had already commenced treatment were recruited as it was anticipated that they would already have an understanding regarding the fundamentals of obesity treatment such as planning and goal setting. In addition, we did not exclude participants based on their level of literacy so that the needs of all users could be taken into account. Overall, the results of testing were promising and participants rated the app as important for them and easy to use. Each of the test tasks were completed successfully without critical error indicating that technical effectiveness was achieved.

The relative user efficiency of the app was compared to that of an expert user and the time taken for novice participants to complete tasks was one to three times that of the expert user. As recommended by Bevan [24], measuring the relative user efficiency highlights the potential usability gap between typical users and an expert user and it is anticipated that it often takes normal users two or three times longer to complete a task than an expert. Users were satisfied with the app and reported a number of ways to improve the app further, which were implemented by the developer. A global SUMI score of 64 was promising as 50 is an average score and 68% of software falls within one standard deviation of the mean (ie, scores between 40 and 60) on the SUMI.

To our knowledge, this was the first study to report on the development and usability testing of a mobile app to be used as an adjunct to adolescent obesity intervention. Given the popularity of mobile apps with adolescents and the limited access to evidence-based treatment, we anticipated that a mobile app would be a useful tool for obesity treatment and the results of this study support this. Strengths of the study include the participation of end users in the iterative development process and our use of validated methods for testing.

Few studies have been conducted to assess the usability of mobile app with adolescent patients. One recent study explored the usability of a mobile app for measuring pain in children with cancer [26]. Similar to our findings, participants in the Stinson study [26], commented positively on the aesthetics of the app, on the rewards system, and future use of the app. Testing also revealed important changes to development that were necessary in order for the pain app content to be completely interpreted by adolescents and to avoid navigating away from a chosen page mistakenly. With regard to user satisfaction, participants completed a questionnaire and 86% reported that they liked using the pain app while 79% reported that they found it user-friendly. These results suggest that the app could be used as a tool to assist adolescents in making decisions around pain management. In a similar study involving adult patients with type 2 diabetes mellitus, 25% of participants expressed frustration with using a mobile app as part of their care due to errors in functioning of the app [27] and a systematic review of apps for diabetes management revealed that the look and feel of the app could impact the perceived usefulness of the app [28]. Considering our study against the background of the above study, it is clear that usability testing is paramount for the optimal design and development of mobile apps used in clinical cohorts.

Limitations

Although the test sample for this study might be considered small in number, a minimum of 8 participants is recommended in heuristic usability testing [29]. We recruited 12 participants for the study but on the day of testing, 2 families could not attend. Given that testing was undertaken with a group of adolescents attending a single urban hospital for weight management, the results cannot be generalized. Future study is

warranted to test the usability of the app with a larger number of participants. In addition, the app should be tested in a cohort of adolescents who are not attending a clinic for weight management, as we do not know whether the user's level of motivation for lifestyle change affects their perceptions regarding technical usability.

In addition, as the testing was undertaken in one building using the same WiFi network, we could not ascertain whether the technical effectiveness could be guaranteed when users are dispersed across the 3G network. However data regarding such limitation will be collected in the ongoing clinical trial. In addition, the clinical trial will reveal whether adolescents engage with the app in a "real-life" scenario over a 12-month period and whether there is a dosing effect with regard to use and effect on health outcome. Finally, we assessed satisfaction of using the app as a whole rather than satisfaction with completing each particular task. Future work to explore each individual component of the app may also be warranted.

Conclusions

Overall, the Reactivate mobile app performed well in usability testing and the results provide support for its usability by end users. Results of this study guided the final development cycle of the app prior to its use in a randomized controlled clinical trial (NCT01804855). The usability testing of mobile apps designed to address clinical problems is vital, as the needs of the user can be taken into account for better optimization of the mobile app, with respect to its acceptability and utility.

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We thank the adolescents and their parents for choosing to participate in this study and are also thankful to the research assistants Fiona Ward, Robert Rusk, and Richard Lambe. We thank Dr Jurek Kirakowski and Dr Tadeusz Kirakowski for their assistance with the SUMI. Funding related to this project was granted to the principal investigator by the Health Research Board of Ireland (HRB) and the Children's Fund for Health through the HRB clinical research fellowship. The sponsors were not involved in the preparation or review of this manuscript. Finally, we would also like to thank the Vodafone Foundation for provision of a test site.

Conflicts of Interest

None declared.

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Abbreviations

BMI: body mass index
HRB: Health Research Board
ISO: International Organization of Standardization
RUS: relative user efficiency score
SUMI: standardized software usability measurement inventory

O'Malley et al. Trials 2014, 15:43
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TRIALS

STUDY PROTOCOL Open Access

A smartphone intervention for adolescent obesity: study protocol for a randomised controlled non-inferiority trial

Grace O'Malley[1,2,7*], Mike Clarke[3], Amanda Burls[4], Sinéad Murphy[5], Nuala Murphy[6] and Ivan J Perry[2]

Abstract

Background: There are few evidence-based mobile health solutions for treating adolescent obesity. The primary aim of this parallel non-inferiority trial is to assess the effectiveness of an experimental smartphone application in reducing obesity at 12 months, compared to the Temple Street W82GO Healthy Lifestyles intervention.

Methods/design: The primary outcome measure is change in body mass index standardised deviation score at 12 months. The secondary aim is to compare the effect of treatment on secondary outcomes, including waist circumference, insulin sensitivity, quality of life, physical activity and psychosocial health. Adolescents with a body mass index at or above the 98th percentile (12 to 17 years) will be recruited from the Obesity clinic at Temple Street Children's University Hospital in Dublin, Ireland. W82GO is a family-based lifestyle change intervention delivered in two phases over 12 months. In the current study, participants will be randomised for phase two of treatment to either usual care or care delivered via smartphone application. One hundred and thirty-four participants will be randomised between the two study arms. An intention-to-treat analysis will be used to compare treatment differences between the groups at 12 months.

Discussion: The results of this study will be disseminated via open access publication and will provide important information for clinicians, patients and policy makers regarding the use of mobile health interventions in the management of adolescent obesity.

Trial registration: Clinicaltrials.gov NCT01804855.

Keywords: Obesity, Smartphone, Adolescent, Behavioural intervention, Mobile health, Telemedicine

Background

Childhood obesity in Ireland is a major problem: 19% of 9-year-old children are overweight and 7% are obese [1]. Child and adolescent obesity is associated with multiple physical and psychological co-morbidities [2] and, although effective treatments are available, there is considerable room for improvement. For example, a Cochrane Review reported sufficient evidence for the treatment effect of well-targeted interventions and its meta-analyses found a reduction in body mass index standardised deviation score (BMI SDS) of 0.14 at 12 months [3].

The Temple Street W82GO Healthy Lifestyles programme (W82GO) is a family-based multidisciplinary outpatient treatment for child and adolescent obesity (http://w82go.ie/). In a prospective study of the W82GO programme, significant reductions in BMI SDS have been described after 12 months of treatment [4]. However, although the beneficial effects of face-to-face family-based treatment have been described [5], it remains uncertain whether such treatments can be effective when delivered to potentially greater numbers using a mobile health approach.

Data exist regarding the use of technology [6] and mobile applications in a variety of clinical areas, including patient support [7], smoking cessation [8], diabetes management [9], and cardiac rehabilitation [10], but there is a dearth of data regarding the use of mobile health approaches in the management of adolescent obesity.

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Aim

The primary aim of this project is to assess the impact of a smartphone application compared with usual care on BMI SDS over 12 months in adolescents who are obese (12 to 17 years). Secondary outcome measures are waist circumference, insulin sensitivity, quality of life, physical activity and psychosocial health.

Methods/design

Trial design

Randomised trial of 12 months duration with parallel groups and assessor blinding.

Participants

Children and adolescents attending Temple Street Children's University Hospital in Dublin Ireland for obesity management will be recruited. Children are referred to the obesity clinic by their general practitioner, or primary healthcare team.

Eligibility criteria

- Inclusion criteria: child aged between 12 and 17 years, child BMI >98th percentile, child fluent in English, parent(s) willing to participate in the programme with their child and completion of written informed consent and assent prior to any study-specific procedures.
- Exclusion criteria: severe intellectual difficulties which would limit the child's ability to engage in group activity, obesity secondary to genetic condition, limitations to engaging in physical activity (for example, active musculoskeletal injury) or use of medication known to effect body weight, limitations to using a smartphone device and known family issues that would affect general compliance and attendance at follow-up visits.

Recruitment

Children will be recruited from medical clinics and given written information regarding the study. Families wishing to participate in the study will be asked to complete parental consent and age-appropriate child assent forms. The motivation and expectations of both adolescents and parents will be evaluated and the alternative treatment options will be discussed (such as 1:1 treatment in outpatient clinic). It will be made clear to parents and their adolescents that by participating in the study they will have a 50:50 chance of being treated in a standard manner or with the smartphone intervention for phase 2 of treatment.

Based on our calculations, we will need to recruit 134 adolescents for randomisation over an enrolment period of 18 months.

This study will be conducted in agreement with the 'Declaration of Helsinki'. The study has ethical approval from The Children's University Hospital Ethics Board (11–033). All parents and adolescents will give their written informed consent. Modifications to this study protocol will be communicated to all those involved in the study: data monitoring committee, trial steering committee, clinical team, study sponsor, and study funders.

Randomisation

Adolescents who are eligible will be randomised to either a W82GO (usual care) group or a smartphone experimental group by the research team using a secure online randomisation system with full allocation concealment. They will be stratified by gender and parental obesity, and 134 adolescents will be randomised in total using a 1:1 randomisation ratio. After randomisation, adolescents will receive a study code, which will be used to analyse all the data related to that child.

Intervention

Assessment

In keeping with routine practice, adolescents and their parents are assessed by the multidisciplinary team, which allows the team to build trust with the family. Assessment by the multidisciplinary team includes the following.

Paediatrician During this visit, general information is collected concerning pregnancy, birth, and early childhood development. The medical history of the family and the child is discussed along with any concerns that the child or parents have. The causal effects of obesity are discussed along with the medical complications that exist.

The physical examination investigates the presence of acanthosis nigricans, possible dysmorphic features, and hirsutism. Pubertal status is recorded according to Tanner and laboratory tests are requested.

Dietitian In this visit, the nutritional intake of the child is detailed in tandem with the eating behaviours of the family. The child is given a food diary to be completed over two weekend days and one weekday in order to provide an indication of micro- and macro-nutrient intake. The session is also used to introduce information regarding nutrition and healthy eating behaviour.

Physiotherapist The adolescent undergoes a physical examination to screen for musculoskeletal problems (for example, impaired gait or balance) and to measure physical activity levels, blood pressure, sedentary behaviour, sleep, cardiorespiratory fitness and quality of life.

Psychologist This session provides an opportunity for the family to discuss their motivations for becoming healthier. The role of the parent is highlighted and practical strategies to promote a positive environment at home are discussed. Issues such as body image, bullying and self esteem are assessed.

Outcomes

Primary outcome

Anthropometric parameters Body weight is measured to the nearest 0.1 kg using an electronic scale (SECA, Vogel & Halke, Hamburg, Germany) and height to the nearest 0.1 cm with a stadiometer (SECA, Vogel & Halke) in light clothing and without shoes. Measures are taken in triplicate and mean values calculated. Waist circumference is measured with an anthropometric tape midway between the lower rib margin and the iliac crest at the end of gentle expiration. BMI is calculated as weight/height squared (kg/m^2). Subjects are classified as obese if they plot above the 98th percentile for BMI on the Irish growth charts. The primary outcome, BMI SDS, is calculated using UK reference data (Cole LMS method).

Secondary outcomes

Blood sample analysis Blood samples are taken by venipuncture after an overnight fast by an experienced paediatric phlebotomist. Fasting samples are taken to measure glucose, insulin, total cholesterol, high density lipoprotein, low density lipoprotein, triglycerides, thyroid function, glycated haemoglobin, and the liver enzymes aspartate transaminase and alanine transaminase.

Insulin resistance The Homeostasis Assessment Model for insulin resistance formula [11] is used as an index of insulin resistance:

$$(\text{fasting insulin}(\text{mU/ml}) \times \text{fasting glucose}(\text{mmol/l}))/22.5$$

Blood pressure Blood pressure measurements (Omron, Kyoto, Japan) are taken in a relaxed sitting position, in triplicate. The last measurement is used for analyses [12].

Physical activity Objective measurement of physical activity will be completed using 7 days of accelerometry data (Geneactiv accelerometer, Activinsights, Kimbolton, UK). The Physical Activity Questionnaire for Adolescents will be used to measure subjective physical activity in adolescents. This is a 7-day self-report measure, which is reliable and valid for use in adolescents aged 7 to 19 years [13].

Physical fitness Cardiorespiratory fitness is measured with a submaximal treadmill test (modified Balke test) with heart rate, rate of perceived exertion and oxygen saturation monitoring [14]. The test takes between 10 and 15 minutes or until 85% of the maximum heart rate is achieved.

Musculoskeletal screen The physiotherapist screens the musculoskeletal system in order to identify any issues that might cause physical limitation to the child. The screening procedure has been detailed in full previously [15]. If there are musculoskeletal concerns identified, the symptoms will be treated as appropriate. Motor skill is evaluated using the balance and coordination subscale of the Bruinnincks Oteresky Test of Motor Proficiency (Pearson, TX, USA).

Health-related quality of life The Pediatric Quality of Life Inventory is used as a measure of health-related quality of life and has been used in obese cohorts previously [16].

Psychosocial health Social, behavioural and emotional functioning is assessed using the Child behaviour Checklist/Youth Self Report [17] and self concept by The Piers Harris Questionnaire [18].

Treatments

W82GO is underpinned by behavioural change theory (transtheoretical model and social cognitive theory) and uses strategies including stimulus control, self-monitoring, positive reinforcement, goal setting and problem solving to facilitate lifestyle change. The intervention is described in full in Additional file 1. W82GO consists of phase 1 and phase 2 treatments.

Phase 1 treatment

Phase 1 is the initial intensive phase and consists of six weekly sessions (0 to 6 weeks) for adolescents and their parents. These sessions last 2 hours and incorporate educational and practical sessions to increase physical activity, improve nutrition, increase sleep and reduce obesity.

Phase 2 treatment

Phase 2 is a maintenance phase. Upon completion of phase 1, participants return with their parents for three 3-monthly booster maintenance sessions over 46 weeks [4]. These sessions are aimed to encourage the family to continue with lifestyle change and to manage barriers to change.

In the current study, having completed phase 1 of treatment, participants will be randomised for phase 2 to either usual care or smartphone care.

The smartphone application incorporates evidence-based behavioural change tools such as self-monitoring, goal setting, and peer support. Evidence-based tips are sent to the user in the form of a text tip, a video tip or an image tip. The tips aim to increase the knowledge of the participant with regard to healthy eating, physical activity, physical fitness and sleep. The user is encouraged to engage in daily goal setting to increase physical activity level and sleep, increase water intake, reduce intake of sugar and fat and to increase intake of fibre, fruits and vegetables. In addition, the user is encouraged to monitor their progress by reviewing their goals daily and by entering their height and weight measurements (which are charted over time).

Those randomised to usual care will return for three booster sessions and for measurement of primary and secondary outcomes at 6 and 12 months. Those in the smartphone group will use the smarphone app and will return for measurement of outcomes at 6 to 12 months. Contact with the participants will be ensured throughout the study by monthly phone-calls from the principal investigator. See Figure 1.

Power calculation

This study is a non-inferiority trial to determine whether a smartphone intervention could be used as a treatment in adolescent obesity management. The null hypothesis is that the smartphone intervention will have a positive effect on BMI SDS but that this change will be inferior to usual care. Based on a 0.21 reduction of BMI SDS at 12 months, a standard deviation of 0.24 in the usual care group and a non-inferiority limit of 0.12, the sample size required at 80% power will be 50 per group or 100 total. To allow for expected dropout the total number of adolescents to be recruited will be 134.

Blinding

After randomisation and assignment to the study group, participants will be given a study identification number. The assessor of the primary outcome will not know the allocated intervention for the participant, to reduce the risk of bias. Given the nature of the intervention, it is not possible to blind the participants or the care providers. An independent data analyst will be blinded during the trial by the use of a fully anonymised dataset.

Electronic health considerations

Given the dynamic nature of electronic health trials, there may be changes to the methodology after trial commencement and, if so, these will be detailed in full. Examples include major bug fixes in the software, changes in the functionality or content of the application and any unexpected events that might influence study outcomes (such as system failures or downtimes).

Data collection and management

Primary and secondary outcome measurement will take place during initial baseline assessment, at 6 months and at 12 months. Participants who drop out of the trial will be invited to attend these follow-up visits for measurement. Data will be stored on password-protected firewalled computers, which are accessible only to members of our research team and those involved in managing the application software. Blood samples will be labelled with the patient's initials and medical record number and stored in laboratories that are locked when not in use. With the permission of the participant (or parent/guardian), the blood samples and information collected during this research study may be stored indefinitely and used by our research group for future studies. Any information about individual participants derived from the additional studies will be kept confidential. The participant may at any time request that the blood samples be destroyed. When the results of the research are published or discussed in conferences, no information will be included that would reveal the identity of any participant unless their specific consent had been obtained. Data will be entered using double-data entry to assure quality control.

Data analysis

All statistical analyses will be performed using SPSS (version 20, IBM, NY, USA). Descriptive statistics will be used to characterise demographic, clinical and laboratory variables. Distributions of primary and secondary outcomes will be examined using histograms and box plots for evidence of deviation from a normal distribution. If the distribution of a continuous outcome variable shows skewness or other marked departure from normality, mathematical transformations will be applied before using inferential techniques that require normality or alternative non-parametric methods (for example, bootstrap). An intention-to-treat analysis will be used to measure change in BMI SDS over time between the two groups and data will be adjusted for baseline age, BMI and gender.

Data monitoring

A data monitoring committee will insure oversight of the trial and will meet with the principal investigator quarterly. This will provide independent review as to whether study participants are being exposed to unreasonable risks and will monitor study progress and integrity. The data monitoring committee will meet to review data from the ongoing trial (outcome data and data regarding adverse events) and make recommendations to the trial steering committee. Data will be managed in accordance with Temple Street Children's University Hospital and UCC data protection policies. Any identifiable information that is obtained in connection with this study will

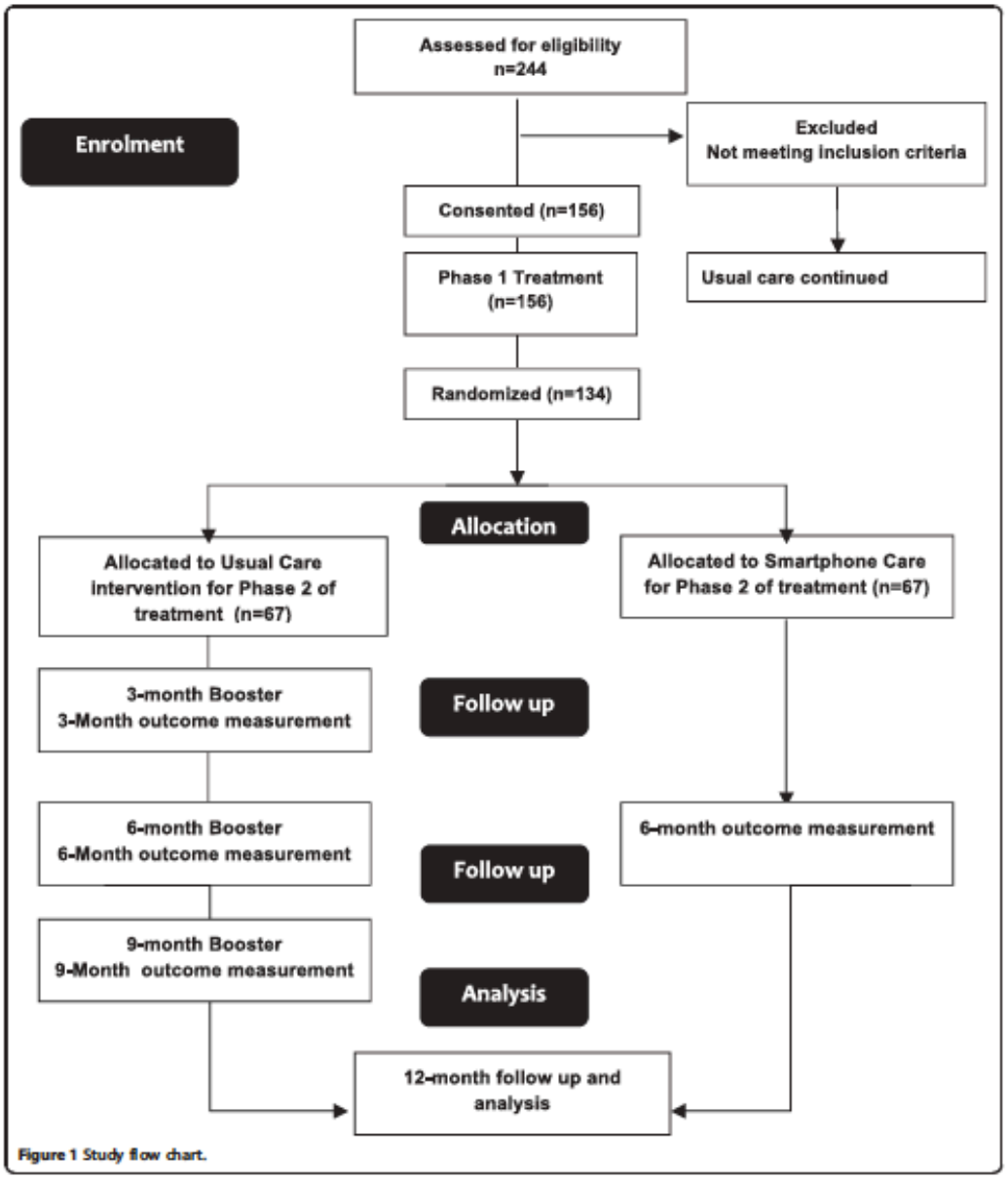


Figure 1 Study flow chart.

remain confidential and will be disclosed only with the participant's permission or as required by Irish or EU law.

Adverse events

At each visit, participants and their parents will complete an adverse events form in order to capture any unintended effects of the trial. Spontaneous reporting of adverse events will be possible by calling the study phone line.

Discussion

The results of the trial will be communicated to study participants, research collaborators, funders and the

general public via a scientific publication and lay summary. The findings are expected to guide further development of a telemedicine system for the management of clinical obesity in adolescence. Ethical concerns specific to telemedical interventions have been considered such as the provision of web-enabled devices to minors, ensuring the security of patient data via online systems, and the use of devices in healthcare delivery which may expose a child to radio-frequency electromagnetic fields.

Trial status

Recruiting.

Additional file

Additional file 1: Describes the full content of the evidence-based Temple Street W82GO Healthy Lifestyle Programme using a modified intervention mapping approach.

Abbreviations

BMI: body mass index; SDS: standardised deviation score; W82GO: Temple Street W82GO Healthy Lifestyles programme.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

GOM, MC, SM and IJP are responsible for the design of the study and contributed to the intellectual content of the protocol. GOM and AB are responsible for the design and development of the smartphone app. GOM and SM are responsible for the implementation of the intervention, data collection, data analysis and drafted the study protocol with suggestions and contribution of all other authors. GOM, IP and NM obtained financial support. All authors read and approved the final manuscript.

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[Intervention Protocol]

Incentive-based interventions for increasing physical activity and fitness

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

The main aim of the review is to determine the effectiveness of using incentive-based approaches (IBAs) (financial and non-financial) to increase physical activity in community-dwelling children and adults.

A secondary objective will be to address the use of incentives to improve cardiovascular and metabolic fitness.

A final objective will be to explore:

- whether there are any adverse effects associated with the use of IBAs for increasing physical activity;
- whether there are any differential effects of IBAs within and between study populations by age, gender, education, inequalities and health status; and
- whether the use of disincentive/aversive approaches leads to a reduction in sedentary behaviour.

BACKGROUND

The World Health Organization (WHO) has recommended a shift of focus from the treatment of illness to one whereby health is promoted. Such a paradigm shift emphasises the need to modify health risk factors including smoking, unhealthy diet and physical inactivity (WHO 2002; WHO 2005). Improving participation in health-enhancing physical activity is of huge importance, as participation in such activity is associated with the prevention of many chronic diseases, including type 2 diabetes, cardiovascular disease, coronary heart disease and some cancers (Bauman 2004; Penedo 2005). Exploring the relationship between physical activity and cardiometabolic health has been the aim of two previous Cochrane reviews (Jolliffe 2001; Thomas 2006).

The reported global prevalence of 'some but insufficient physi-

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cal activity' of 41% is estimated to be associated with 1.9 million deaths, 19 million Daily Adjusted Life Years (DALYs) and approximately 22% of coronary heart disease prevalence globally (WHO 2002). In the United States, less than 5% of the population are reported to engage in recommended levels of physical activity (Troiano 2008), and inadequate physical activity is the fourth leading attributable risk of death (Danaei 2009). Physical inactivity is therefore, not only a major public health burden, but also a significant economic encumbrance (Scarborough 2011). A previous Cochrane review has explored the effectiveness of interventions used to promote physical activity in adults, and observed the use of strategies such as financial incentives in primary studies to modify physical activity behaviour (Foster 2005). Examples of such incentives include free access to private fitness facilities, personal training, supervised exercise sessions and subsidised public transport (Ogilvie 2008). Studies using such incentive-based approaches (IBAs) to increase physical activity behaviour have drawn from research in areas of behaviour modification such as drug misuse (Olmstead 2007; Sindelar 2007), and have been used in behavioural interventions, as part of a suite of strategies, to encourage behaviour change. The commercial world has adopted and refined these principles to make product choice more attractive (Blythman 2004). The repackaging of these approaches in "nudge" theory has awakened interest in utilising the processes of choice architecture "that alters people's behaviour in a predictable way, without forbidding any options or significantly changing their economic incentives" (Thaler 2008). Governments and policy makers have adopted these principles and are currently investigating their application across different policy areas. Nudge type strategies are composed of elements from a number of different psychological theories of behaviour change (social cognitive theory, transtheoretical model and the health belief model). The efficacy of such approaches remains unknown and our review will quantify if these approaches have any impact in physical activity interventions.

Description of the condition

This review will evaluate studies that report on the effectiveness of IBAs to increase physical activity. Physical activity is any bodily movement produced by skeletal muscles which results in increased energy expenditure (Caspersen 1985). Physical activity is associated with indices of health-related physical fitness such as cardiorespiratory fitness, muscle strength, bone strength, balance, co-ordination, flexibility, metabolic
and psychological profile (Bailey 1999; Deforche 2003; Faigenbaum 1999; Katzmarzyk 1998; Malina 2001; Miller 2010; Pate 1990). Although increasing physical activity levels is a cornerstone of obesity prevention and management, it is clear that independent of any effect on body weight, the physical and psychological benefits justify the promotion of physical activity in all humans.

It is recommended that adults engage in a weekly target of 150 minutes of moderate intensity cardiorespiratory exercise training (Garber 2011). In children (5 to 17 years of age) the current recommendations are to accumulate an average of at least 60 minutes per day, and up to several hours, of at least moderate intensity physical activity (Janssen 2010). It is reported that in general, physical activity decreases with age, particularly in females, and that activity level is influenced by biological factors (Rowland 1998), physical limitations (O'Malley 2010), time spent in sedentary pursuits, peer-group activity and individual motivation (Haerens 2009).

Description of the intervention

We will use the socioecological framework to guide our definition of where IBAs can be delivered (Sallis 1999). The socioecological framework describes the interaction between policy, the environment and individual level factors upon physical activity behaviour. Our definition of IBAs reflects these different levels of influence on behaviour. IBAs will include strategies that offer financial or non-financial rewards and incentives at the time of, or after the adoption of physical activity. IBAs can act at an organisational level (e.g. within a workplace), or at an individual level (e.g. payment or rewards for being active for the individual, or payment of healthcare professionals to deliver activity interventions). We will take into account the timing that the IBA is applied, given the negligible benefit that is reported with the provision of tax rebates to those of lower socioeconomic status (Spence 2010). As such, we will consider IBAs that are provided before or after initiating physical activity.

It is hypothesised that by applying IBAs, an increased awareness of the health-promoting physical activity message may ensue, in tandem with improvements of knowledge regarding the benefits of activity, increases in the motivation to be active, as well as improved attitudes and beliefs related to becoming physically active. Such developments might improve participation in physical activity and reduce sedentary behaviour in an effort to take advantage of the IBA, while facilitating improved levels of physical fitness and reductions in morbidity and mortality.

This review will also consider the negative consequences associated with the use of IBAs. It has been reported that the use of IBAs may have unintended repercussions, such as undermining intrinsic motivation or eroding an individuals' decision-making autonomy (Claassen 2007; Deci 2009). There are additional ethical and moral concerns regarding whether the use of IBAs is coercive or inequitable (Gostin 2007; Halpern 2007); this review will attempt to report on such issues of concern.

The study will encompass any strategy or item that could be deemed as a reward by the study recipient, to facilitate motivating study participants to increase their participation in physical activity. This will include taxation rewards, grant opportunities, subsidies and reduced price opportunities to be active, salary bonuses, direct financial payments, lottery tickets, competition entries and

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prizes. Similarly we will include disincentives and aversive approaches for sedentary behaviour, such as penalties or increased taxes for undertaking actions which would otherwise lead to sedentary behaviour. Such penalties will include the use of fines where traffic calming strategies are ignored by motorists, or car parking costs. Car-free zones, 30 km/hr speed limits, parking capacity limitations and high taxation of automobile ownership and use have been used in many urban areas to promote and facilitate pedestrian and bicycle traffic.

How the intervention might work

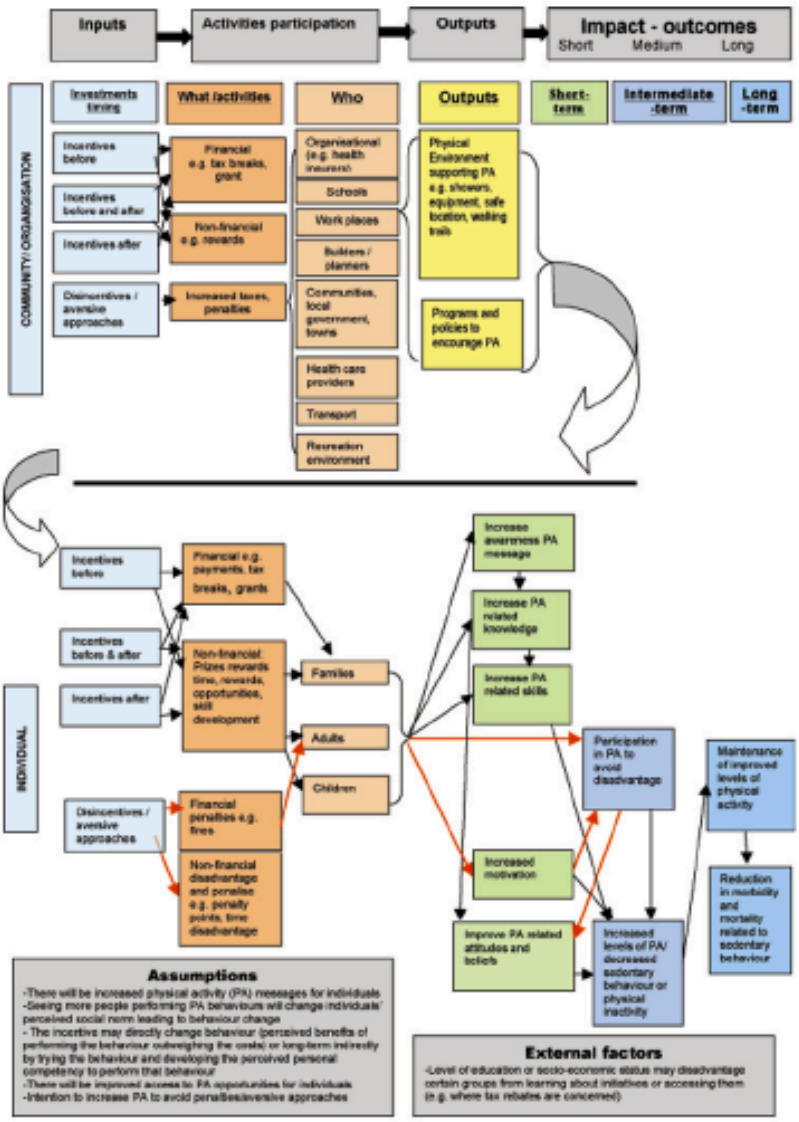
Research on decision-making has found that the desire to avoid regret is a potent force in decision-making (Connolly 2006), as is the incentive value of small rewards and punishments (Ainslie 1975). The theory underpinning how IBAs might work, draws from psychological, ecological and behavioural economics research. It is proposed that individuals consider an IBA with a present bias and may want to do what is in their long-term interest (become more active), but usually succumb to the temptation to be sedentary. People may be more patient in immediate future choices than in distant future choices (Loewenstein 1992; Thaler 1981). As such, an IBA may facilitate an individual to pursue a smaller, more immediate reward (e.g. payment for participating in a work-based exercise class) instead of a more distant but valuable reward, for example, avoiding chronic illness by participating in ongoing physical activity (Berns 2007). Similarly, the use of IBAs facilitates the removal of barriers (cognitive and physical) to participating in physical activity, and such modification of attitudes and motivation may lead to changes in behaviour and action.

Disincentives and aversive approaches for sedentary behaviour might be used to reduce sedentary behaviour (i.e. congestion or high parking charges to reduce car use and increase walking). Whether an associated increase in physical activity is elicited by reducing sedentary behaviour is not clear (Pate 2008); we will explore if this is the case in the review. To date, researchers propose that by targeting theoretical constructs such as individual behavioural processes, self-efficacy, and social support, a change in the behavioural outcome (i.e. physical activity) may be observed (Lewis 2002). A 2008 Cochrane review investigated the use of incentives for the promotion of smoking cessation and concluded that none of the trials included showed higher quit rates at six months when incentives were used (Cahill 2008). More recently, a large trial conducted by Volpp 2008, showed a positive effect of using personal financial incentives on sustained quitting at 12 months. Regarding physical activity interventions, recent data proposes a promising benefit for the use of IBAs in well-designed studies (Kahn 2002; Lewis 2002; Vandelanotte 2007). Identified studies may use payment or an incentive to encourage study participation and this may have a varying degree of impact, particularly in cohorts at a socioeconomic disadvantage. As such, we will aim to address such issues of inequity and reach.

We have developed a logic model (Figure 1) to show the two levels at which incentive interventions may be directed, i.e. at the community/organisational level, or directly at the individual level where intermediate- and long-term activities are expected to be observed (Foster 2005). The activities participation stage describes the type of IBA that is used, at what time it is applied, in what setting it is used and to what target group it is offered. It is hypothesised that the use of the IBA will lead to a variety of outputs such as changes in the physical environment and the implementation of policies and programmes directed at increasing physical activity. Such outputs will impact upon a variety of outcomes ranging from the short- to the long-term. Such outcomes could include increased awareness of health-promoting initiatives, an increase in knowledge related to the benefits of physical activity, improvements in motivation, increased participation in physical activity and subsequent reductions in morbidity and mortality. We will use the logic model to describe the components of the intervention which may have influenced a change in behaviour (activity level).

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Figure 1. Logic model for IBA used to increase physical activity



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Why it is important to do this review

It is important to increase population levels of physical activity related to lifestyle choices in order to address the increasing burden of chronic diseases (e.g. type 2 diabetes and cardiovascular disease). To date, the use of IBAs in a variety of settings to increase physical activity has been promising (Kahn 2002; Lewis 2002; Vandelanotte 2007). In the absence of a systematic synthesis of the evidence regarding the use of IBAs for the promotion of physical activity, recent national policy has supported their use (e.g. in England, the Step2Get programme) (Healthy Lives 2010). A Cochrane review of community-wide interventions examined only interventions which were multi-strategy in nature (Baker 2011), and thus did not address IBAs as a distinct strategy, which is the focus of this review.

It is currently unknown whether using incentives is more effective in the promotion of sustained physical activity, compared to not using incentives. Promotion with incentives is the focus of our review, however we acknowledge that there are examples of incentives offered to community organisations to encourage specific actions (e.g. subsidies to promote the building and development of public spaces which prioritise walking and cycling). At present we feel these actions lie beyond the scope of our review. In addition, it is unknown whether certain incentives are more effective than others in promoting health-enhancing physical activity and associated measures of fitness. Equally, it is unknown whether disincentives for sedentary behaviour can lead to an increase in physical activity. As such, it is warranted that the evidence to date is synthesised in an effort to guide the implementation of future strategies. Finally, we acknowledge that an incentive may be viewed differently by individuals or groups in various settings and as such, we will identify and explore such issues in the qualitative description of the included studies.

OBJECTIVES

The main aim of the review is to determine the effectiveness of using incentive-based approaches (IBAs) (financial and non-financial) to increase physical activity in community-dwelling children and adults.

A secondary objective will be to address the use of incentives to improve cardiovascular and metabolic fitness.

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METHODS

Criteria for considering studies for this review

Types of studies

We will include all randomised controlled studies (RCTs) comparing the use of incentives for the promotion of physical activity with a minimum follow-up of 12 weeks in community- dwelling children and adults. Although the inclusion of non-RCTs will increase the susceptibility for bias, we will include non-RCTs and time-series studies with comparator groups because we anticipate that a limited number of RCTs will be available. We will include two component reviews in order to examine the evidence, which pertains to both RCTs and non-RCTs. We will include studies that have compared the use of an incentive to increase physical activity in one group versus the use of no incentive in the other. The intervention component of included studies could be a once off intervention, or an intervention extending over a specified length of time. We will only include studies that measure physical activity levels (using standardised subjective or objective tools) pre- and post-intervention.

Types of participants

We will include studies that include community-dwelling children (< 18 years) and adults (> 18 years). We will exclude studies in which athletes or sports students participate.

Types of interventions

We will define incentives as 'any strategy that offers financial or non-financial rewards (before, and or after physical activity) in an effort to facilitate motivating the study participants to increase their participation in physical activity'. As IBAs could be applied in a number of settings, we will use the logic model (Figure 1) to classify the type of intervention and at which level (community or individual) it is utilised. In addition, we will include studies testing the use of disincentives or aversive approaches.

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The following are examples of IBAs, which might be utilised in order to increase levels of physical activity, consistent with the logic model to be included in this review.

Community Level

- Financial incentives offered by health insurers or other bodies to employers who provide wellness programmes to employees.
- Grants and support for establishing walking-school buses.

Individual Level

- Tax rebates for individual purchases of exercise equipment or club memberships.
- Time-for-time; prizes; competition entries or bonuses to staff who participate and sustain physical activity via employer provided or after work wellness programmes.
- Academic incentives and credits offered to students who increase their participation in physical activity.
- Subsidies offered to individuals for purchasing a bicycle through, for example, a 'bike-to-work' scheme.

Disincentives or aversive approaches

- City congestion charges; fines to motorists who park or drive in bicycle lanes; increase in fines to motorists who speed in populated areas; the use of penalty points to drivers who disregard cyclist and pedestrian safety; and no-car zones.

Types of outcome measures

We will include studies if physical activity level is either a primary or secondary outcome of interest.

Primary outcomes

The primary outcome will be physical activity level assessed by standardised tools between baseline and follow-up. Studies should employ objective measures of activity such as pedometers and accelerometers (Webber 2008) or subjective measures such as self-report and validated questionnaires (Jeffery 1998).

Secondary outcomes

We will include secondary outcomes of cardiovascular fitness (e.g. risk factors such as blood pressure, blood lipid profile and aerobic capacity); metabolic fitness (e.g. insulin sensitivity and glycaemic control); musculoskeletal fitness (e.g. muscle power, flexibility and the presence of pain); mental health (e.g. symptoms of depression and anxiety); measures of motivation; and quality of life measures.

We will also detail additional outcomes such as financial (e.g. data relating to cost effectiveness, cost per unit change in outcome and cost-benefit analyses) and adverse effects (e.g. perceptions of coercion, undermined intrinsic motivation and data indicating inequity), as well as information detailing the specific psychological theory underpinning the intervention.

Search methods for identification of studies

Electronic searches

We will search relevant multiple databases and websites (as recommended by Armstrong 2008) using a sensitive search strategy developed by GO'M in liaison with the Public Health Group's Trials Search Co-ordinator, and will tailor the MEDLINE strategy for each database during 2012. In the month, prior to submission of our review, we will check all the highest yielding databases for newly published studies. We will handsearch the reference lists of review articles and included studies and contact experts in the field for other potentially eligible studies. We will impose no language or date restrictions in our search. We will search the following databases for material.

Health

Cochrane Public Health Group Register
CENTRAL
MEDLINE
EMBASE
CINAHL
PsycINFO
PUBMED
PEDRO
LILACS
Web of Science
Cochrane Occupational Health Field Register

Business

EMERALD
Business Source premier
EconLit

Architecture, sport, transport and planning

Avery
Compendex
GEOBASE
SPORTDiscus
TRIS

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Social sciences

Sociological abstracts
ASSIA
C2-SPECTR (Campbell collaboration)

Grey literature

HMIC
OpenSIGLE
Index to Theses
ZETOC
In addition, we will search the WHO International Clinical Trials Registry Platform (WHO ICTRP) to identify studies in progress.

Searching other resources

In addition to databases, we will search other resources for published and unpublished studies.

- We will handsearch our top 10 high yielding journals (those which yield the highest numbers of studies that meet the inclusion criteria), such as *The American Journal of Preventative Medicine, Preventative Medicine* and the *ISBNPA Journal*, if these have not already been handsearched by The Cochrane Collaboration.
- We will search reference lists of all papers and relevant systematic reviews that have been identified as meeting the inclusion criteria for the review.
- We will conduct a Google Scholar search for relevant material and search key websites (International Labour Organisation, WHO and International Network of Agencies for Health Technology Assessment).
- We will contact subject experts through the International Society for Physical Activity and Health, HEPA Europe (European network for the promotion of health-enhancing physical activity) and the Active Living Research Organization.

Data collection and analysis

Selection of studies

We will divide the resulting titles from the search by the review authors for initial screening by GO'M and DF. IP, PB, or CF will independently examine the title, keywords and abstract of each report for inclusion in the review. We will import article records from each database into the bibliographic software package Endnote 2010, where we will remove duplicates and select relevant articles. We will undertake an initial screening of titles and abstracts to remove those which are obviously outside the scope of the review. The review authors will be over inclusive at this stage and, if in doubt, we will include a paper. We will obtain the full text for the papers potentially meeting inclusion criteria (based on the title and abstract only), and we will link together multiple publications and reports on the same study. The review authors will not be blinded with respect to authors' name, journal or date of publication during this process. Multiple review authors (GO'M and shared between IP, PB and CF) will screen all the full text papers obtained and will utilise the logic model (Figure 1) to assess whether basic components of the definition of an IBA and permissible study designs are fully met. Where there is a persisting difference of opinion, DF will review the paper in question in order to reach a consensus between the review authors. We will maintain a record of the outcome of the study assessment process for all reviewed material. After the initial selection, GO'M and CF will perform a re-screening of a random 10% of all excluded titles to ensure no suitable titles have been omitted.

Data extraction and management

Two review authors (GO'M and either DF, IP, PB or CF), will independently complete a data extraction form for each study, tailored to the requirements of this review. GO'M, DF and CF will pilot the data extraction form to assess its ability to capture study data and inform assessment of study quality. We will resolve any problems identified through discussion and we will revise the form, as required. Where studies report more than one endpoint per outcome, we will extract the primary endpoint identified by the authors. Where the review authors do not identify a primary endpoint, we will rank the measures by effect size and extract the median measure (Curran 2007). Should there be relevant study reports in languages that cannot be translated by the review team, GO'M will complete the data extraction form in conjunction with a translator.

We will extract relevant data from all full text studies meeting the inclusion criteria and assess them for study implementation and fidelity using the quality assessment criteria that corresponds to the RE-AIM public health intervention evaluation framework. These include: 'reach', or the number and representativeness of programme participants; 'efficacy/effect' of the intervention on important positive or negative outcomes; 'adoption', or number and representativeness of settings and intervention agents; 'implementation', or consistency, quality and resources required in programme delivery; and 'maintenance', the institutionalisation of the intervention into routine practices or policy. We will use a check list to ensure inclusion of data relevant for health equity (Morris 2009). In addition, we will assemble multiple reports and publications of the same study and compare them for completeness and possible contradictions. We will mark on the logic model (Figure 1) the specific components present in the primary paper and companion publications to assist in the categorisation of studies and interpretation of results, where heterogeneity is present. We will manage numerical data for analysis that is extracted from the included studies, in a Microsoft Excel spreadsheet.

GO'M and IP will cross-check the completed data extraction forms

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for consistency and should any discrepancy arise, we will seek consensus through discussion. GO'M will file and store all copies of studies undergoing data extraction and completed data extraction sheets (including printed versions of electronic forms) in a filing cabinet for auditing and checking purposes. We will transfer data for collation from our data extraction sheets to RevMan 5.1 (RevMan 2011); IP will independently check the accuracy of this procedure. Where necessary, we will contact study authors to provide data that may be missing from the study reports or to resolve any uncertainty about reported information. We will record any study that undergoes the data extraction process and is subsequently rejected from the review summary in the 'Characteristics of excluded studies' with a rationale for non-inclusion. In addition, we will also present relevant information on all included studies in the 'Characteristics of included studies' table.

Using the location of the intervention, we will categorise the studies as occurring in low-, middle- and high-income countries, as determined by the World Bank classification.

We will review all papers and reports of included studies to identify whether any description of costs or resources were made by the authors. Information extracted will include descriptors of cost to deliver the intervention over the time specified. Where possible, we will separate the cost of the intervention from the cost of the evaluation and research components. Where the results are presented at a population level, we will calculate the cost per person. We will identify and include in kind support. We will also extract general statements (e.g. "low cost intervention") made by the authors, where no expression of monetary value is made.

Assessment of risk of bias in included studies

GO'M and PB will assess the risk of bias. We will assess the studies meeting the inclusion criteria using the Cochrane 'Risk of bias' tool (sequence generation; allocation concealment; blinding of participants and personnel; blinding of outcome assessors; incomplete outcome data; selective outcome reporting; and other sources of bias) (Higgins 2011a). Analysis of non-RCTs will follow the guidance provided in the Effective Practice and Organisation of Care (EPOC) 'Risk of bias' documentation and we will develop a risk of bias table (EPOC 2009). We will judge studies to be at 'low', 'medium', or 'high' risk of bias given overall consideration of the study design, size, and the potential impact of the identified weaknesses. Where there is disagreement between review authors in risk of bias assessment, DF will appraise the study independently and we will resolve discrepancies by consensus between all review authors.

Measures of treatment effect

We will analyse studies with continuous outcome measures using the mean and standard deviation (SD). If not possible, we will report only the point estimate with confidence intervals (CIs) and P values. We will express the effect sizes for dichotomous outcomes as risk ratios (RRs) in the first instance. For continuous outcomes, we will use weighted mean differences (WMDs) between the post-intervention values of the intervention and control groups to analyse the size of the effects of the interventions.

Unit of analysis issues

If a study has more than two arms that are relevant for inclusion in the review, we will examine the overall effects of the intervention versus control by pooling the intervention arms into one group to create a single pair-wise comparison. For continuous outcomes, we will calculate and weight the mean and SDs according to the overall numbers within each arm using the formulae in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011b). For dichotomous outcomes, we will calculate odds ratios (ORs) with 95% CIs, and we will use the number of participants in each arm that are reported as an event (categorised at a pre-determined level) or no event (for example, not active).

This approach is more appropriate than comparing the effects of (one intervention arm versus control) and (the second intervention arm versus control), within a meta-analysis, as the same participants cannot be included twice in the comparison and effect calculations. Where appropriate, we will calculate individual study effects and then the pooled effect sizes as ORs with 95% CIs using a random-effects model. We will calculate any missing 95% CIs using approaches outlined by (Deeks 2011).

We will re-analyse, if possible, studies which randomise or allocate by clusters but do not account for clustering during analysis. Where the population reporting attainment of a physical activity level is stated as a percentage of the population meeting a specified attainment level, we will consider the analysis as being at the same level as allocation for each cluster. Alternatively, if appropriate, we will employ statistical methods that allow analysis at the level of the individual while accounting for the clustering in the data. If successful, effect estimates and their standard errors (SEs) from correct analyses of cluster-randomised trials may be meta-analysed using the generic inverse-variance method in RevMan 5.1 (RevMan 2011).

Dealing with missing data

We will contact the authors of potentially included studies if missing data are unclear or data have not been fully reported. We will capture missing data in the data extraction process and report it in the risk of bias table.

Assessment of heterogeneity

We will initially assess the differences between included studies. We will use the logic model (Figure 1) in the categorisation of the type of intervention strategies included, participants and outcomes. We will quantify and evaluate the amount of heterogeneity to

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determine whether the observed variation in the study results are compatible with the variation expected by chance alone (Higgins 2003). We will assess heterogeneity through examination of the forest plots and quantify it using the I^2 statistic. We will perform a sensitivity analysis to investigate heterogeneous results.

Assessment of reporting biases

PB will plot trial effect against SE using funnel plots (Sterne 2011). Given that asymmetry could be caused by a relationship between effect size and sample size, or by publication bias (Egger 1998), we will examine any observed effect for clinical heterogeneity and we may carry out additional sensitivity tests.

Data synthesis

We will report continuous outcomes on the original scale, where possible. If the outcomes are to be combined from different scales we will standardise these as required for the analysis. We will only undertake a meta-analysis when data are clinically homogeneous. We will follow Chapter 9: 'Analysing data and undertaking meta-analyses' in the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2011). GO'M, DF and CF will perform statistical analyses using RevMan 5.1, if all available data are sufficiently similar, and of sufficient quality (RevMan 2011). We will use a random-effects model to incorporate heterogeneity among studies that cannot be explained, to ensure it is clear that this model does not remove the need to try to explain causes of heterogeneity. We will not combine evidence from differing study designs and outcome types in the same forest plot (Christensen 2009).

In the situation where it is not appropriate to conduct a meta-analysis, we will develop a table with effect sizes of each study. In addition, we will present the median effect size and its range for each outcome. We will conduct a narrative synthesis of the results as a means of considering the included interventions and the body of evidence identified through the review process.

Subgroup analysis and investigation of heterogeneity

We will make an assessment whether to pool RRs by measuring the effectiveness of incentive-based intervention compared to no intervention on physical activity, following initial assessments of methodological heterogeneity. Where sufficient data are available, GO'M, DF and CF will perform additional subgroup analyses to compare outcomes by: types of study designs; group effects for people who share a common social, cultural, or health status characteristic (age, gender, ethnicity); reach of intervention; and intensity of intervention (derived from use of the logic model and process evaluations). The subgroup analysis will also explore whether there is any evidence of differential effects of the intervention by socioeconomic and demographic group. Where appropriate, we will assess subgroup heterogeneity through examination of the forest plots and quantification using the I^2 statistic.

Sensitivity analysis

We will carry out sensitivity analysis to explore the impact of risk of bias on study findings by repeating the meta-analysis that excludes studies that are assessed as having a high risk of bias.

Summary of findings

GO'M and PB will prepare a summary of findings table for the primary outcomes related to physical activity and sedentary behaviour using GRADE profiler (Schunemann 2011). We will summarise the quality of evidence by applying the principles of the GRADE framework and following the recommendations and worksheets of EPOC for creating summary of findings tables (EPOC 2011). We will use four levels of quality (high, moderate, low and very low) to describe the body of evidence. We will create the table using the measures for the primary outcomes identified as being most important, most reliable and the most predominant. We will assess the quality of evidence for each outcome across studies. Non-randomised studies will start at low quality; however given the a priori expectation that the highest quality of evidence is likely to come from large, controlled before and after studies of communities, we will not further down-grade such studies if we identify deficiencies in randomisation. We will assess the magnitude of the effect, sample size, representativeness of the population cohorts, and the validity of the measures used to determine whether it is appropriate to upgrade or downgrade the quality of a finding. We will also consider information from process and evaluation reports of the intervention. The primary determinant for upgrading or downgrading the evidence will be whether the issues identified are likely to affect the outcome based on the logic model and the GRADE criteria.

The summary of findings table will contain illustrative comparisons of the effect of the intervention upon population levels of primary outcomes using three scenarios of physical activity levels and intervention approaches that are indicative of low-, middle- and high-income countries. If necessary, we will adjust the illustrations for any corresponding equity gradient that may be apparent, such as the staircase effect (Tugwell 2006). This may identify an increasing gap and decreasing effectiveness by advantaged and disadvantaged populations across relevant components of the intervention. We will quality assess the prevalence data used in the comparison using the framework of Loney 2000. We will minimise multiple reporting of measurement instruments for physical activity and sedentary behaviour that cannot be combined, to ensure the size of the table is proportionate to the quantity of meaningful findings. We will base the selection of measurement instruments upon known validity aspects of the instruments and the prevalence of their use in the primary studies. Interpretation of the findings will emphasise potential population and health policy significances, rather than solely clinical significance. In the event that meta-analysis is not appropriate, we will prepare an alternative

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summary of findings table using narrative analysis of the included studies.

ACKNOWLEDGEMENTS

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APPENDIX III.
CONFERENCE ABSTRACTS PUBLISHED DURING THE PH.D. CANDIDATURE

- O'Malley G, Killeen S, Murphy S. Are balance and quality of life impaired in children who are obese? Appetite. 2014; 76(0): 198.
- O'Malley G, Brinkley A, Mooney K, McInerney M, Murphy S, Killeen S, Murphy N. Establishing a hospital based obesity service: An Irish Experience. Obesity Facts 2012;5(S10):9.
- O'Malley G, Brinkley A, Moroney K, McInerney M, Murphy S, Killeen S, Murphy N. Is the Temple Street W82Go Healthy Lifestyles Programme effective in reducing BMI SDS? Obesity Facts 2012;5(S10):223.

31 invited speaker

ESTABLISHING A FAMILY-BASED OUTPATIENT TREATMENT: AN IRISH EXPERIENCE

G. O'Malley[1], A. Brinkley[1], K. Moroney[1], M. McInerney[1], S. Murphy[1], S. Killeen[2], J. Butler[1], N. Murphy[1]

[1] THE CHILDREN'S UNIVERSITY HOSPITAL, Physiotherapy Department, Dublin, Ireland Republic of

[2] CENTRE FOR HEALPUBLIC RESEARCH CENTRE FOR HEALTH (CRP-SANTÉ), Physiotherapy Department

Abstract Text: Introduction: The W82GO Healthy Lifestyles programme is a family-based multidisciplinary treatment for children who are obese (>98th BMI percentile). **Methods:** Throughout its development, families have contributed to the design, delivery and evaluation of the programme. This presentation discusses the broad demographic profile of families attending W82GO and how the family situation can influence treatment efficacy. The challenges and highlights of delivering an outpatient-based obesity programme will be described along with strategies used to tailor treatment to a variety of user needs. The central role of the family and parental attitude towards lifestyle change will be discussed and particular attention will be given to the importance of communication within the healthcare team and between the team and the families involved. Conclusions: Delivering an effective outpatient based obesity intervention poses a number of challenges which should be considered during programme design and evaluation.

Conflict of Interest: The authors report no conflict of interest.

Funding: Research relating to this abstract was funded by The Children's Fund for Health at The Children's University Hospital, Dublin, Ireland.

833 accepted poster

IS THE TEMPLE STREET W82GO HEALTHY LIFESTYLES PROGRAMME EFFECTIVE IN REDUCING BMI SDS?

G. O'Malley[1 2], A. Brinkley[3], K. Moroney[4], M. McInerney[5], J. Butler[6], N. Murphy[6]

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[2] UNIVERSITY COLLEGE CORK, Public Health, Cork, Ireland Republic of

[3] THE CHILDREN'S UNIVERSITY HOSPITAL, Metabolic Unit, Dublin, Ireland Republic of

[4] THE CHILDREN'S UNIVERSITY HOSPITAL, Dietetic Dept, , Dublin, Ireland Republic of

[5] THE CHILDREN'S UNIVERSITY HOSPITAL, Nursing, Dublin, Ireland Republic of

[6] THE CHILDREN'S UNIVERSITY HOSPITAL, Paediatric Endocrinology Section, Dublin, Ireland Republic of

Abstract Text: Introduction: The W82GO Healthy Lifestyles programme is an evidence-based multidisciplinary treatment for children who are obese. W82GO aims to improve nutrition, physical activity and fitness levels, and facilitate behaviour modification. This study describes the changes in BMI SDS in those treated in W82GO. **Methods:** A retrospective audit of patients referred from Sept 2005-April 2011 was conducted to describe the changes over 12 months. A univariate analysis correcting for gender, baseline age and BMI SDS was used. **Results:** 219 children were referred and 164 accepted treatment (88 boys). Those who refused treatment were younger (6.88 years versus 11.08 years, p=0.004). Mean characteristics of participants were: age 11.07 years [95% CI 10.57, 11.57]; BMI 31.23 [30.34, 32.13]; BMI percentile 98.82 [98.65, 98.98] and BMI SDS 2.41 [2.34, 2.47]. 148 participants completed 6-months of treatment and 98 completed 12 months (drop-out of 18% and 40%). There were no baseline differences between those who participated and those who dropped out. BMI SDS decreased by 0.07 [0.05,0.09] at 6 months [F=6.93, p <0.001] and by 0.16 [0.12,0.21] at 12 months [F=5.84, p =0.001]. No gender differences were observed however BMI SDS of younger children (<6 years) decreased more than older children at 12 months (-0.43 versus -0.13 [6-12 years, p<0.001] and -0.14 [12-16 years, p<0.001). Conclusions: W82GO significantly reduced the BMI SDS in youth who were obese.

Conflict of Interest: The authors report no conflict of interest.

Funding: Research relating to this abstract was funded by The Children's Fund for Health at The Children's University Hospital, Dublin, Ireland.

835 accepted poster

LIFESTYLE INTERVENTION IN WOMEN WITH EARLY-STAGE, NON-METASTATIC BREAST CANCER: RATIONALE AND DESIGN OF THE LIFESTYLE MODIFICATION PART OF THE SUCCESS-C STUDY

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[3] HEINRICH-HEINE UNIVERSITÄT DÜSSELDORF, Department of Gynecology and Obstetrics

836 accepted poster

LONG-TERM DETERMINANTS OF VISCERAL FAT LOSS AND STABILIZATION IN HIGH-RISK ABDOMINALLY OBESE DYSLIPIDEMIC MEN WITH FEATURES OF THE METABOLIC SYNDROME

J. A. Nazare[1], A. L. Borel[2 1], J. Smith[1], I. Lemieux[3], N. Alméras[1], J. Bergeron[4], A. Tremblay[1], P. Poirier[1], J. P. Després[1]

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[2] HÔPITAL UNIVERSITAIRE DE GRENOBLE, Grenoble, France

[3] CENTRE DE RECHERCHE DE L'INSTITUT UNIVERSITAIRE DE CARDIOLOGIE ET DE PNEUMOLOGIE DE QUÉBEC

[4] CRCHUL, Québec, Canada

Abstract Text: Introduction: SYNERGIE was a lifestyle intervention program for the clinical management of men with features of the metabolic syndrome (MetS) combining: 1) a one-year abdominal fat loss phase (healthy eating, exercise/physical activity (PA), 2) a two-year weight stabilization phase, both based on a personalized counselling by health professionals. **Methods:** We aimed to identify which intervention components (PA, caloric/macronutrient intake, diet quality score (DQ) assessed by 3-day dietary and daily PA journals/pedometer) were related to the loss and stabilization of visceral adiposity (VAT, assessed by computed tomography). From the 144 initially recruited subjects (age: 48±9 y, waist circumference: 108±8 cm, triglycerides: 2.52±0.89 mmol/l), 117 viscerally obese men completed the first year, and 94 (65%) the third year of intervention. **Results:** After one year, the decrease in VAT (-26%, p<0.0001) was significantly and independently associated with the significant changes in PA (reported exercise, daily number of steps) and in DQ score, but not with changes in reported total caloric intake (-559±68 kcal/day) or diet macronutrient composition.After the 2 year-weight stabilization phase, the subjects who lost the most VAT after one year still presented a significantly lower VAT after 3 years compared to baseline, despite the highest VAT regain and independently of diet or PA parameters. The subjects who lost the least VAT after one year were not different at year 3 from baseline. Conclusion: These results emphasize the need to synergistically focus on both PA and DQ to optimally reduce VAT over the long term in viscerally obese men with the features of the MetS.

Conflict of Interest: None

Funding: This study was supported by the Canadian Institute of Health Research: CIHR grant 89985.

837 accepted poster

MEASURING PHYSICAL ACTIVITY IN > GRADE 2 OBESE PATIENTS

J. Franklin[1], E. Manson[1], G. Loughnan[1], T. Markovic[1]

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Early psychopathology of obesity. A study with preschoolers and their parents. A. EK [a], J. HEDMAN [b], C. MARCUS [a], P. NOWICKA [a,c]. [a] *Division of Pediatrics, Department of Clinical Sciences, Intervention and Technology (CLINTEC), Karolinska Institutet Huddinge, B62, 141 86 Stockholm, Sweden,* [b] *Department of Public Health Sciences, Karolinska Institute, Stockholm, Sweden,* [c] *Unit for Biocultural Variation and Obesity, School of Anthropology and Museum Ethnography, University of Oxford, Oxford, UK.* anna.ek@ki.se

While increased levels of depression and symptoms of ADHD have been reported in older children with obesity, not much is known on the prevalence of early psychopathology in obese children as young as four. Parents' to 4–6 year old children ($n = 28$, mean age 4.9 yrs, 50% boys) with obesity (mean BMI SDS 3.0), participating in a treatment study, filled out the Child Behaviour Checklist for ages 1.5–5, measuring the child's emotional, social and behavioural problems. The parents also filled out the Beck Depression Inventory Second Edition (BDI-II), measuring parents' degree of depression. Children's levels of problematic behaviour symptoms were compared to Swedish and Danish reference populations. The total score of problem behaviours in this clinical sample was 30.6 (SD 20.3), compared to 22.3 (15.4) for Sweden and 16.1 (15.0) for Denmark. Obese children had higher scores on the following subscales: externalizing, internalizing, affective problems, anxiety, attention and depression. They were more withdrawn and had more sleep problems than their normal weight peers. Mothers' scores on BDI-II were positively correlated with the children's scores on the total problem scale and on the externalizing problem subscale ($p > 0.000$). The results were adjusted for child's age at the onset of obesity as well as parent's ethnicity. The high prevalence of psychological problems as early in life needs to be confirmed in larger samples.

http://dx.doi.org/10.1016/j.appet.2014.01.017

Restrictive feeding and child weight. Evidence for a bi-directional association in preschool children. P.W. JANSEN [a,b], V.W.V. JADDOE [a], A. HOFMAN [a], F.C. VERHULST [a], H. TIEMEIER [a]. [a] *Erasmus Medical Centre, PO Box 2060, 3000 CB Rotterdam, The Netherlands,* [b] *Murdoch Children's Research Institute, Melbourne, Australia.* p.w.jansen@erasmusmc.nl

Parents' restriction of food intake has consistently been associated with a higher body mass index (BMI) in children. It is assumed that parental restriction weakens children's self-regulation, but restriction may also be a parent's response to child overweight. With few exceptions, studies have not examined this possibility. In longitudinal analyses, we aimed to identify directionality in the restrictive feeding–BMI relationship among preschoolers. BMI was measured among 3478 children in the population-based Generation R Study. Restriction (Child Feeding Questionnaire) was self-reported by parents. Bi-directionality was examined in a path analysis with Restriction and BMI expressed in standard deviation (SD) scores. Path analysis jointly estimating Restriction–BMI associations in both directions and accounting for continuity in BMI over time indicated that a higher BMI at age 2 years was associated with more restriction at age 4 years, which in turn was positively related with child BMI two years later. However, associations were modest, e.g. for each SD increase in Restriction, child BMIz increased by 0.07 (95% CI: 0.04, 0.10). The relation from BMI to parenting was stronger than reverse (Wald test for comparison: p-value = 0.03). Our results imply a bi-directional relation between restrictive feeding and child BMI. This suggests that, in contrast to school-age children, among preschoolers a cyclical relationship may appear: the main direction of effect was parents responding to high child weight by restriction of food intake, while excessive restriction may also have a small counterproductive effect resulting in overeating and adiposity.

http://dx.doi.org/10.1016/j.appet.2014.01.018

Are balance and quality of life impaired in children who are obese? G. O'MALLEY, S. KILLEEEN, S. MURPHY. *Weight Management Service, Temple Street Children's University Hospital, Dublin 1, Ireland.* omalleyg@tcd.ie

Children who are obese have impaired physical fitness. Balance and coordination are key parameters of fitness and when impaired can lead to falls and musculoskeletal injury. The aim was to investigate whether children who are obese have impaired balance and to explore whether balance impairment is associated with quality of life. Children were recruited from an obesity clinic and were classified as Class 1 (C1) obese (BMI SDS 2.0–2.49) or Class 2 (C2) obese (BMI SDS > 2.5). Balance was measured using the BOT-II. Based on age-adjusted norms, children were classified as having a balance impairment. Quality of life was assessed using the PedsQL. A general linear model compared the differences in balance between C1 and C2 with correction for age, gender and musculokeletal injury. A t-test compared quality of life between children with and without balance impairment. Eighty-seven children (11.15 ± 2.7 years) who were obese (mean BMI SDS = 2.36 ± 0.32; C1: $n = 57$) were recruited. Mean balance was 26.52 ± 5.2 out of a maximum of 37. 71.26% Of children had impaired balance (C1 70.18% C1; C2 73.33%). C2 obese children had lower balance scores compared to C1 obese children ($F = 5.27$; $p = 0.02$). Mean quality of life was 59.0% ± 19.8% (C1 60.7% ± 19.1; C2 57.44 ± 19.8) and children with balance impairment had lower quality of life (56.43 ± 18.35 versus 66.88 ± 20.68, $p = 0.04$). Results of our study indicate that balance was impaired in children who were obese and that children with such impairment had a lower quality of life. Results highlight the importance of conducting a physiotherapy assessment in children who are obese.

http://dx.doi.org/10.1016/j.appet.2014.01.019

APPENDIX IV.
INVITED PRESENTATIONS DURING THE PH.D. CANDIDATURE

OP: Oral Presentation, PP: Poster presentation

- 2014 OP: Clinical Effectiveness of a Smart Phone Intervention for Adolescent Obesity: Preliminary results. ATA 2014, Baltimore, USA.
- 2014 OP: Royal College of Physicians in Ireland. Obesity Master class: Multi-disciplinary management of childhood obesity –from W82GO to web 2.0
- 2014 OP: Connected Health Seminar University of Ulster. Obesity and Diabetes
- 2014 PP: Balance and quality of life in children who are obese. International Congress on Obesity, Malaysia.
- 2014 OP: MRC Clinical Trials All-Ireland Hub. From bench side to curb side: maximizing obesity research to impact health.
- 2013 OP: The Role of Physiotherapy in Childhood obesity. SOPAC; American Pediatric Physical Therapists Annual Congress; California, USA
- 2013 OP. Balance Impairment in childhood Obesity. 23rd European Childhood Obesity Group Meeting, Liverpool UK
- 2013 PP Exploring the Usability of a Smartphone Application for Adolescent Obesity Management. Medicine 2.0 London, UK.
- 2013 OP: Obesity Treatment & technology; Oxford University & City University London, UK
- 2013 OP Technology in Healthcare. British Society for Paediatric Rheumatology, Dublin.
- 2013 OP Using remote devices for the delivery of obesity interventions. HRB/Safefood
- 2012 OP Establishing a hospital based obesity service: An Irish Experience. ECO 2012, Lyon, France
- 2011 OP Tracking metabolic change with changes in body composition in children with obesity. World Congress of Physical Therapy, Amsterdam, Netherlands.

APPENDIX V.
RELATED SCIENTIFIC ARTICLES PUBLISHED BY THE CANDIDATE

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Acceptability of an evidence based Smartphone application for adolescent obesity treatment

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Abstract

Background: Research carried out by Wooldor Et al 2011 demonstrated the acceptability of SMS texting to adolescents attending an obesity management program. It has been shown that evidence-based Smartphone applications may assist in reducing obesity by extending access to effective treatment. It is imperative that such applications are developed in line with the existing evidence-base and consider the needs of the end-user throughout the development process.

Aim: This study aimed to collect qualitative data regarding the acceptability of a Smartphone application used for the support and on-going remote treatment of adolescent obesity.

Method: Parent-adolescent dyads attending the W82GO healthy lifestyles programme were invited to participate in the study. Two semi-structured interviews and two focus groups for ten parents and ten young people between 13 and 16 years of age were convened to collect qualitative data regarding the content and usability of a smartphone application to be used in childhood obesity management. Participants discussed what types of websites they liked to visit, limits on their access to the internet, what an

app designed for obesity treatment should look like and what it should contain. social media component.

Results: Main themes reported by parents included the benefit of peer support and concern regarding social networking aspects of the application. Parents expressed concerns about online bullying from peers and predatory behaviour from adults both online and off line. Adolescents suggested a number of strategies to protect their identity when online use the app. Adolescents had clear ideas relating to the design and usability of the application and how it could be used as a supportive tool. Finally, data highlighted the digital divide between parents and adolescents in use of the Internet and Smartphone applications.

Introduction

Obesity is considered as a global epidemic, with more than one billion adults world wide overweight, and 300 million considered clinically obese. It is estimated that half a million adults in Europe and North America die from obesity related conditions (World Health Organisation, 2002). Childhood obesity is an increasing global concern with an estimated 22 million children affected (Ref). Between 1995 and 2003 the number of overweight children aged 2-10 years in the United Kingdom rose from 22.7% to 27.7%. In a 2006 study authors reported that 17.8% of children aged 4-13 years were overweight with 6.8% clinically obese (Jotangia, Moody, Stamatakis, & Wardle, 2006). The recent Growing up in Ireland study revealed that 19% of nine year olds were considered overweight, and seven percent were obese (Layte & McCrory, 2011). Short-term consequences of childhood obesity include, joint pain, low physical fitness, high blood pressure, early signs of cardiovascular and metabolic disease, low self esteem, and depression (O'Malley et al 2012a; Bell et al,2011; O'Malley et al 2010; D'Adamo et al., 2010; Finucane et al., 2008, Tounian et al., 2001). Long-term consequences include a greater likelihood of being an obese adult and a greater risk of cancer, Type 2 diabetes and cardiovascular disease (Guo et al., 2002).

There is sufficient evidence to justify well-targeted treatment of children with obesity (Oude Luttikhuis et al., 2009; NICE 2010) and meta-analyses indicate that treatment can results in a clinically meaningful reduction in obesity (Oude Luttikhuis et al., 2009). The evidence to date does not support one form of treatment over another, however behavioural lifestyle interventions are the most appropriate for the paediatric and adolescent populations**.**

Achieving such clinically significant change with treatment can be challenging and many barriers to adhering to treatment interventions have been reported. Such barriers include financial constraints lack of resources (transport, childcare; information, access to physical activity; family support); and safety concerns (Sonneville, et al., 2007; Williams et al 2010). It is recommend that design of effective interventions should involve the end users and consider the needs of families (Sonneville, et al., 2007; Williams et al 2010).

W82GO is a family-based treatment intervention for children and adolescents who are obese. It is delivered by a multi-disciplinary team and has been described in detail elsewhere (O'Malley et al. 2012b). Beneficial reductions in obesity have been reported however access to the treatment is restricted due to limited resources (O'Malley et al 2012c). In an effort to increase on-going support for families involved in W82GO, accessing treatment a smartphone application has been designed to provide a remote treatment option.

72% of Irish households have access to the Internet at home (AMAS, 2011b). Moreover web-enabled mobile devices such as smartphones and tablet computers are becoming ubiquitous. Smartphones act as computing devices and incorporate utilities including the Internet, camera functions; accelerometry and Global Positioning System (GPS) facilities. In excess of five billion people worldwide own a mobile phone (Hampton, 2012). The global penetration rate is 87%, with 79% in the developing world (International Telecommunication Union, 2011) In 2011 the number of

Smartphones in use in Ireland increased to 741,000, this consisted of 326,000 android phones, 219,000 iPhones and 233,000 other brands with 27% of owners under the age of 24yrs. (AMAS, 2011c). Computer aided communication has shown to be helpful in e-mentoring teenagers with special needs (Shpigelman, Reiter, & Weiss, 2008). An analysis of a German online service for people with an eating disorder found it could provide a suitable first point of contact for patients and their families. The research found that 57% of contacts to the service described themselves as having an eating disorder, 32% had friends or relatives with a disorder and 9% when looking for information only (Grunwald & Wesemann, 2007). The use of short messaging services (SMS) texts to support behaviour change has been found effective in post partum Australian mothers (Fjeldsoe, Miller, & Marshall, 2010) obesity treatment in American teenagers (Woolford, Barr, Derry, Jepson, Clark, & Resnicow, 2011; S. J. Woolford, Clark, Strecher, & Resnicow, 2010). To date telemedicine options have been used in a variety of areas including mental health (Pretorius et al., 2009; Laffen, 2012); to support behavioural change in post-partum mothers (Fjeldsoe, Miller, & Marshall, 2010); for adolescent obesity treatment (Woolford, et al., 2011; Woolford et al., 2010), in diabetes management (Armstrong and Powel, 2009). In 2012, health related smartphone apps are expected to total 13,000 (Dolan, 2011).

Web-enabled devices allow the user to access a myriad of information and recent reports reveal that 80% of Internet users search for health information on line Fox (2011). In the United Kingdom the national Health Services (NHS) Direct Online provides health information and advice for patients (National Health Service, 2011.) , similar facilities are available in Germany and Denmark (Andreassen et al, 2007). Following the success of the NHS experience, the Irish Health Service Executive (HSE) plan to introduce a similar service on their website (396) Appropriately designed telemedical approaches offer both advantages and disadvantages particularly in the area of public health and chronic disease management. The anonymity offered can facilitate the sharing of information between

individuals and can assist in the provision of peer support and validation (Amichai-Hamburger & Furnham, 2007; Caplan & Turner, 2007; Caplan, 2007; Griffithset al., 2006). Disadvantages include the challenge of securing confidential data and privacy (Luxton et al (2011). Currently Internet delivered interventions should be considered as methods of augmenting the clinician-patient interaction rather than methods of replacement (Griffiths, et al., 2006). A review of existing CMC dietary and physical activities in 2007 found mixed results for their effectiveness and recommended evaluation of future interventions to ensure their effectiveness (Norman, Zabinski, Adams, Rosenberg, Yaroch and Atienza, 2007).

Aim:

The current study aimed to explore how acceptable an obesity treatment smartphone app would be to parents and adolescents attending the hospital for face-to-face treatment.

This study tested the following hypotheses;

1. Adolescents would be interested in interacting with a Smartphone application support as part of the W82GO service.
2. Adolescents would expect a high level of interactivity from a Smartphone app.
3. Parents would have limits on the level of social activity and personal information they would be comfortable with their child sharing through a Smartphone app.
4. Adolescents would have definite ideas regarding the design and usability of a Smartphone app.

Methods

Participants

Adolescents (12-16 years) and their parents who were attending the

W82GO service were invited to participate. Participants were excluded if the adolescent resided in foster are; if they had a learning disability or if either the adolescent or parent were not proficient in

Procedure

This research was guided by the ethical guidelines from the American Psychological Association (American Psychological Association, 2010) and the principal investigator's professional code of ethics (An Bord Altranais, 2007). Ethical approval was granted by the Children's University Hospital, Temple Street and the Department of Learning Sciences Ethics Committee at the Dun Laoghaire Institute of Art, Design and Technology.

The study utilised qualitative research methods to explore the lived experiences of parents and adolescents attending for obesity children in order to inform the design of a Smartphone app. A qualitative approach was employed as its flexibility allowed exploration with the subject in a holistic manner through focus groups and field notes (Polit, Beck, & Hungler, 2001). An information leaflet and an invitation to attend a focus group were distributed to 44 families who had attended the obesity service in the past or were currently attending. To ensure parents and children fully understood the process and to ensure informed consent, all letters to parents and children were written in line with recommendation of the national Adult Literacy Agency. The language used was in plain English, aimed at a reading age of 12 yrs. with the minimal use of jargon (397).

Parent and adolescent focus groups took place in the evening on alternate weeks during the month of April 2012. In line with recommendations, each focus group contained between six and twelve participants (Belle Brown, 1999). During the focus groups sessions, the researcher used a topic guide with a number of topics to be explored (Table 1). The discussion concentrated on the use of technology, the Internet and mobile phones. Adolescents were asked what they would expect or like to be included in a Smartphone application to support what they gained through W82GO

program. Each focus group was audiotaped using two digital recorders, one placed on either end of a large table. Participants were gathered around a large table in a comfortable room. The discussion within the focus group was informal and flowed freely. During and after each focus group the facilitator made field notes to capture the mood of the group, their body language and other non-verbal cues. The principal investigator avoided unduly influencing the focus group discussions and as she was not involved in the clinical assessment or management of the participants the potential for bias was reduced. During each focus group the principal investigator paraphrased the discussion back to the group to ensure the content was understood or to clarify any points required.

Any participant who was distressed as a result of taking part in this research was offered an appointment with the W82GO clinical psychologist and in line with the hospitals Child Protection Guidelines any information disclosed that warranted investigation was discussed with the Medical Social Work Manager.

Data collection

Recorded data was transcribed verbatim. Transcripts and the field notes were analysed in detail and an audit trail of all data gathered was maintained.

Data Analysis

Data was analysed from an interpreter's approach, which allowed the research to be viewed from the perspective of the participants. The use of this approach allowed for reflection on findings as they emerged, and for further clarification during the next focus group if required.

As the data was read, the researcher placed memos along the margins to capture the thoughts and impressions of the research each time the data

was read. This allowed for insights and explanations to be recorded (Birks, Chapman, & Francis, 2008). The collected data was classified into five main themes: use of smartphones and apps; use of the Internet; social interaction options, safety and usability and design. Sections of text from the focus groups were represented graphically as a Wordle (a graphic representation of the frequency of words within a body of text generated by a computer algorithm). The graphic was generated on a website www.wordle.net and captured as an image. As the Wordle was not saved within the website but captured in a screen grab no names were used, and confidential information was not shared with a third party.

Results

Ten parent-adolescent dyads participated in the study. The parents group and interview consisted of eight females (80%) and two males (20%) and the adolescent group was comprised of six (60%) females and four (40%) male. Participant characteristics are described in Table 1.

Use of smartphone applications

Throughout the discussions a high level of familiarity with smartphone was found among all participants. Four parents and six adolescents reported owning a smartphone. Initially only one parent (10%) admitted to being familiar with Smartphone apps but later two others spoke about their experiences. Parents proffered comments tentatively as they were aware of the gaps in their knowledge of Smartphone apps in general. All the young people (10 participants) were familiar with phone apps and reported using a number of them on a regular basis. Energetic exchanges were made about the range and use of apps. Those who did not have a Smartphone were familiar with apps through other devices. Adolescents reported a higher level of confidence and familiarity in using Smartphone app than their parents. The types of apps used by adolescents are described in figure 1. All of the adolescents reported using social networking apps which included Skype, Facebook, BlackBerry Messenger (398), Viber, YouTube, Play Station

Messenger (PSM). These applications allow users to communicate with each other free of charge when in a free wireless data exchange (Wi-Fi) area in addition to the possibility of knowing when their contacts are online. The popularity and wide range of apps was reflected in the comments from all participants regarding how they used their apps for communicating with their friends (Table 2[a,b]).

Use of the Internet in the family home

A gap in knowledge level between parents and adolescents existed concerning the use and level of comfort using computers and the Internet in their home. When asked about their personal use of the Internet novice parent users explained the extent of their use. One parent expressed confidence in her Internet skills and one parent also spoke about their child using the Internet for school projects (Table 2[c,d]). Parents acknowledged negative aspects to the Internet and expressed concerns regarding its openness and the availability of Internet services on a wide range of devices, which may not require parental knowledge (Table 2[e,f]).

The unpredictability regarding the suitability or appropriateness of resources located when using search engines was highlighted by two parents (Table 2[g,h]). The ease of communicating with others through the Internet was a source of concern for two mothers (20%) as they were unaware of whom their child may be communicating with (Table 2[i,j]).

Parents spoke freely about concerns for their children as they independently engaged with Internet. It was clear that parents were aware of the ubiquitous presence of the Internet but struggled with how to inform and protect their children from its negative aspects. It was clear from verbal and non-verbal feedback from parents that they were united in their concerns about access to the Internet for children. They struggled with their inexperience while acknowledging the need to provide guidance for their children. Despite their concerns about their children's access and use of the Internet, three parents (30%) acknowledged it usefulness as a resource

when seeking information (Table 2[k]).

Social activity with apps

The possibility of using an app to provide a way of contacting others was explored by both parents and adolescents. Parents were open to receiving support from health professionals associated with their child's obesity intervention via an app which could provide on-going support if required. One mother explained how she would like to have contact to a member of the obesity service through an app as it would provide e-mentoring for the parents if required (Table 3[a,b]). Adolescents did not express a need to contact members of the clinical team. It was suggested by parents that app could be used to provide on-going contact with other parents for peer support and to share tips. (Table 3[c-g]). Another mother acknowledged her concerns of the social networking possibilities using the app (Table 3[h]).

Despite their concerns about social networking via the app parents did acknowledge possible benefits to both themselves and their child (Table 3[i])..
All adolescents were familiar with social networking using services such as Facebook. This seemed to exert a strong influence on how they envisioned contact could be maintained through the app and how they valued the possibility of sharing tips and support with one another (Table 3[j-n]).

Safety and Privacy Issues

Privacy

As experienced social networking users the adolescents were familiar with a number of strategies that could be used to protect their online privacy. Adolescents balanced their desire to contact others with their caution in sharing too much personal information. They demonstrated a level of maturity in acknowledging their need in controlling how and with whom they would share their information. The group offered a number of suggestions on the need for privacy and on how privacy protection could be incorporated into the app (Table 4[a-e]).

Moderated Messages

The possibility to moderating messages to ensure offensive or inappropriate content was not displayed was discussed with adolescents. The group valued instant responses and expected the app to be policed and offensive contributors removed.

Video Diary

When exploring the use of a video diary to share with others, parents were hesitant and guarded (Table 4[f-i]) though mother did give the possibility serious consideration (Table 4[j]).

When asked about posting a video about them one female adolescent replied that she would not be interested in posting video files but did acknowledge they would share "certain photos". Due the reported low self-esteem of the adolescents and nervousness of the parents the function of sharing video images was not a priority for either groups.

Safety

As the app would be developed in collaboration with the W82GO team it automatically engendered trust for one mother (Table 4[k]).

Bullying

Adolescents were aware of the possibility of bullying online. They readily shared a number of strategies that could be utilised to reduce the possibility and suggestions were made on how to hide their offline identity (Table 4[l,m]).

Parental Supervision

Both groups were asked if parents should have access to their child's W82GO app. Some parents (30%) expressed desire to see their child's app and one suggested the choice should be offered to parents (Table 4[n]). The majority of parents (70 %) did not see the need to supervise their child's

app activity for a number of reasons and the other parents did not feel the need to be aware of the contents of their child's app (Table 4[o,q]). Adolescents were strongly opposed to the prospect of parental supervision of the app (Table 4[r]).

Usability and Design

Adolescents had definite ideas on its appearance and navigation and made suggestions about the practical design and usability of the app (Table 5a[a-e]) however parents expressed their difficulty imagining how the app would work and act (Table 5a[f,g]).

Customisation

Adolescents expressed a desire for the app to have a customization function for the user and they had strong ideas on how this could be achieved. They suggested that the app should provide tailored information about the value of different options to assist the user in making suitable healthy choices (Table 5a[h-j]).

Personal Preferences

Adolescents suggested the app should allowing participants to enter demographic information about themselves together with their personal preferences (Table 5a[k-p]).

Content for the App

Adolescents gave suggestions on content for app that would assist them in maintaining the knowledge they had gained during face-to-face treatment (Table 5a[q-s]).

Motivation

All the participants welcomed the possibility of an app designed to provide on-going support for families attending the W82GO service. Participants saw

the app as having a role in promoting physical activity and in acting as a reminder or motivator. Parents suggested also that the app would have a role in supporting their children (Table 5a[t-v]).

Goal Setting

Goal setting was an important part of the W82GO program for adolescents. They explained how the app could help them to set and maintain their individual goals (Table 5b[a,b]).

Tips

Parents considered the app as a valuable tool which could provide tips on ways to encourage their child's healthy lifestyle choices and adolescents suggested the app could also provide random tips to promote healthy lifestyle choices and nutrition (Table 5b[c-h]).

Reminders

Parents welcomed the an app feature which would remind their child of their commitment to certain goals (Table 5b[i,j]), while adolescents described the difficulty in embedding physical activity into their daily life (Table 5b[k-m]).

Sharing App with Wider Public

Both groups explored the possibility of making a W82GO app available to the public. In recognition of the challenges they faced participants favoured sharing the expertise offered by the app however, sharing the app with individuals not associated with the W82GO programme elicited some concerns from both groups. Concerns involved the vulnerability of young people attached to the program and a fear of predation by adults (parents) and bullying by adolescent peers (Table 5b[n-p]). All of the adolescents were happy to share the app with others as they acknowledged the potential benefits in supporting healthy lifestyles and weight obesity management for

children and young people (Table 5b[q,r]). Three adolescents (30%) expressed the desire that others should be helped as they were (Table 5b[s,t]). One adolescent cautioned on its relevance to the wider general public and all adolescents expressed concern about the possibility of negative comments (Table 5b[u-x]). Suggestions were offered by two parents on how the benefits of the program could be open to others yet ensuring protection of the vulnerable children associated with the program (Table 5b[y,z]).

The study hypothesis was tested. Firstly the hypothesis that adolescents would be interested in interacting with a Smartphone application as part of their obesity treatment was supported. Adolescents expressed an interest in using such an app, as they were familiar with goals and methods of treatment in addition to being experienced in using smartphone apps. Secondly, the hypothesis that adolescents would expect a high level of interactivity from a smartphone app was supported. As experienced Internet and Smartphone app users adolescents expected an app to have the functionality of popular commercial apps such as Facebook and Twitter. Thirdly the hypothesis that parents would have limits on the level of social activity and personal information they would be comfortable with their child sharing through a Smartphone app was supported. Parents expressed concerns about their child's personal information being available to others through a Smartphone app due to potential risks of their child becoming a target for bullying by peers or predation by adults. Finally, the hypothesis that adolescents would have definite ideas regarding the design and usability of a Smartphone app was supported. As frequent users of the Internet and Smartphone apps adolescents had definite ideas on the apps usability and appearance.

Sections of relevant text from the focus groups are represented graphically as a Wordle in Figures 2 and 3.

Discussion

Given the increasing use of telemedical approaches in health care and in

particular for reducing the burden of non-communicable disease, the current study sought to inform development work for a smartphone app to be used in adolescent obesity management. In an effort to enhance the participatory involvement of end-users in the design phase, families who were engaged in obesity treatment at a paediatric hospital were recruited. Qualitative data regarding the acceptability of a Smartphone application used for support and on-going remote treatment of adolescent obesity was collected and yielded important insight regarding the expectations and needs of both adolescents and parents. A number of themes emerged from the research and will be discussed.

There was a marked difference in the level of familiarity and comfort using CMC between the young people and their parents. Parents acknowledged their inexperience and some were hesitant to share the extent of their CMC experiences. In contrast their children spoke with confidence describing the extent of their activities.

As smartphones become more sophisticated, their popularity is dramatically increasing, Worldwide they are expected to outsell personal computers by the year 2013 and such popularity may in part be fuelled by the large number and range of apps available (155). Among the participants of this research 60% of young people and 40% of parents owned a Smartphone.

Adolescents discussed their use of CMC for communication with their peers via email or social media. These findings support AMAS (2011a), which reported that 67% of secondary school students used social networking sites, 37% chatted to friends online and 35% use email. Both adults and adolescents in this study indicated that communication should be a component in the proposed app. Both parents and adolescents felt it should be text based, as they were not in favour of the use of a video diary. Both parents and adolescents discussed concerns regarding the safety risks of communicating with others online through an app. Parents expressed concerns about online bullying from peers and predation from adults both online and off line. These fears are validated by research, which highlighted

that 23% of Irish children report being bullied face to face and 4% online. 23% of children surveyed admitted to communication with a person they did not know online and 10% of teenagers met an unknown online contact face to face (O'Neill et al 2011). Given the evidence to date and the concerns of the study group, careful design regarding the moderation of social networking components of a healthcare app is warranted. In addition, it would be important that end-users are fully informed regarding who has access to the app information and data therein contained.

Privacy Online

For a number of years individuals have shared a wide range of information using message boards, signing in using there on line identity. Online sharing of information and peer support by patients has proven useful for people living with chronic conditions (Armstrong & Powell, 2009). In the current study, participants were aware of the need to protect their privacy online. Parents identified the possible threat from adults who might wish to harm their child off line and adolescents identified a possible threat from online bullying in addition to possible negative feedback from their off line peers. Work by O' Neill et al (2011) reported that 12% of 9-16 year olds have had their data misused online, whereby most commonly accounts were hacked and they were impersonated online. In the current study, adolescents suggested a number of strategies to protect their identity when online use the app. If young people were exposed to others that made inappropriate contact it was presumed that such individuals would be excluded from future contact through the app.

Analysis of the adolescent focus group content provided valuable insight regarding expected functionality of an app. Each young participant had definite ideas on what it should contain, how it would look and the level of interaction they expected which was in contrast with the parents who had less familiarity with apps. This divergence in expectation is not surprising considering the high level of app use in Ireland particularly among individuals under of 24 yrs. of age (AMAS 2011b). Within in this study 60%

of young people and 40% of parents owned a Smartphone. Participants within the focus groups considered relevant healthy lifestyle information an important component of a Smartphone app. Adolescents had definite ideas on its design, colour scheme and content. It was important to them that could customise the app to suit their personal taste and schedule. Research findings suggest that websites, which also included chat room facilities, can also provided additional social support to users (Wantland, Portillo, Holzemer, Slaughter, & McGhee, 2004). The desire to communicated with others experiencing similar challenges were reflected in this research. All the adolescents in the current study were experiences users of social networking sites such as Facebook. They expressed satisfaction in how a social networking component to the app would facilitate sharing of content with others and rejected real-time moderation of the app due to expected time delays in uploading information. Though parents were aware of social networking such as Facebook and expressed concerns on how it was used, they did see a benefit in their children communicating with each other via the app.

Participants from both focus groups identified the app as a potential source of valuable e-mentoring through text messaging and pop up messages. The literature supports the use of e-mentoring using mobile devices. Woolford et al (2010) found that young people in an obesity program enjoying receiving text messages, which they found relevant to their lives. Such messaging could enhance motivation and all participants in the current study welcomed the idea of an app providing on-going motivational support from the clinical team. Parents expressed frustration in trying to motivate their children at home and adolescents explained how such functionality could provide them with random tips and reminders of their agreed goals. Woodford et al (2011) found this type of CMC support effective with American teenagers on an obesity management program. Similarly, online support was reported to be beneficial for both young people and parents involved in obesity management as it allowed individuals to disclose as much or as little personal information as they wished (Amichai-Hamburger,

Wainapel, & Fox, 2002).

Valuable insights were gained from this study. A major strength of the study was that it provided an opportunity to services users to participate in the design of a smartphone app that would be used by individuals similar to them. Many challenges exist when involving children and adolescents in research, however, it is important that they are given opportunities to voice their needs and inform the delivery of the service they receive. In this research the adolescents were an inspiration in their enthusiasm and vision for the app. The study is greatly limited by the small study sample and as such the results do not represent the opinion of all families attending the W82GO service for obesity treatment. Nevertheless results do provide an in-depth profile regarding the participants vision for an app to be used as a telemedical device particularly in the area of supporting healthy lifestyle choices, and facilitating motivation and communication between service users.

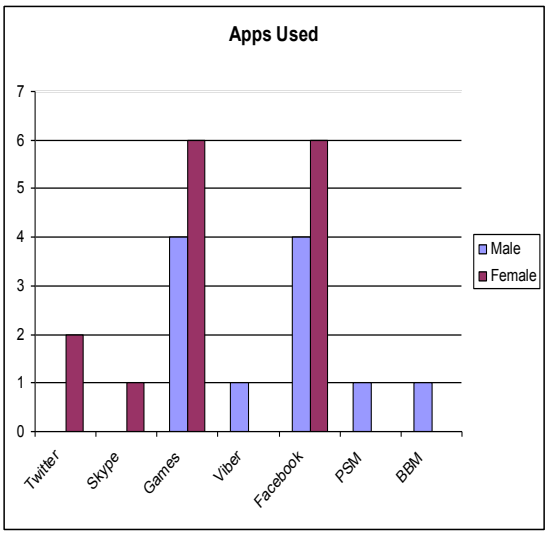
It is clear given the increased availability of free and low cost apps for Smartphones and tablet devices that there is a willingness of individuals to use such apps as lifestyle supports. The emerging area of computer-mediated communication by health professionals to influence health behaviours is in its early development however; the healthcare industry should harness such communication tools with enthusiasm equal to the commercial sector. Despite the number of available apps there is paucity of evidence to support their design or measure their effectiveness. It is recommended that any smartphone apps used to deliver a healthcare monitoring or intervention should follow evidence-based guidelines and standards. The introduction of a quality mark could guide the general public towards using apps that are evidence based. Due to the knowledge gap between parents and adolescents with regard to using smartphone apps, it is essential that training be provided before informed parental consent for their use in treatment is obtained. Following consent for use of apps in treatment on-going support and resources should be provided to parents on

technical aspects and online safety.

Conclusions

The current study yielded valuable data regarding the acceptability of a smartphone app to be used in adolescent obesity management. Data revealed insight regarding the acceptability of internet-based resources for empowering young people and their families to make healthy lifestyle choices. On the whole participants were positive regarding the development of a weight management app and provided useful recommendations regarding design and delivery of such a service.

Figure 1 Types of App Young People Used



BBM (Blackberry Messenger)

Figure 2 Wordle From All Parents Focus Group and Interview

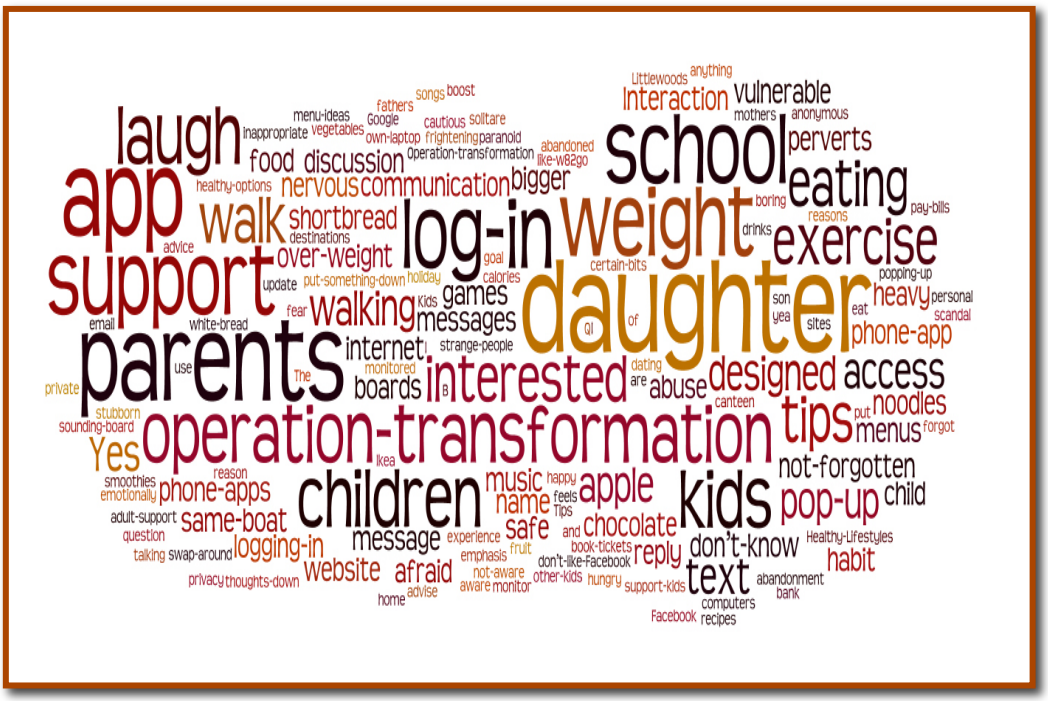


Figure 3 Wordle from Entire Young Peoples Group and Interview



Table 2 Direct comments regarding topic themes 1 and 2

Qualitative theme	Participant Comment
1 Use of Smartphones and Apps	
a) Adolescent male	"…You get it on your iPhone you see who is on line… (399)"
b) Adolescent female	"Twitter and YouTube and I used to like Facebook but I am not on it any more…I like to talk to famous people (Twitter)"
2 Use of the Internet in the family home	
c) Female Parent	". I use banking …I know how to go into my account and pay my bills…– one time I had my dad and we got on to the census 1911 and we went to my fathers family – he loved that "
d) Female Parent	"Well they use it for their school stuff, was on it last night she is doing her junior cert and she needed pictures of art so we were Googling pictures of strawberries "
e) Female Parent	"Kids can go on to sites you are not aware off - Well you don't know what they are looking at."
f) Male Parent	"Now they are going around with these things in their hands as well I don't know much about them either "
g) Male Parent	"And the pop ups…Yea you don't know what is going to pop up"
h) Female Parent	"I remember one of the kids typing in one of the Disney films Snow white or something and I can tell you the amount of things that came up and I can tell you Snow White was not there"
I) Female Parent	"…I try to tell that you know that there is strange people out there… I don't like these dating things and the chat rooms…"
j) Female Parent	"I hate Facebook …there is too much gossip and scandal and people putting things up there that are inappropriate"

Table 3 Direct comments regarding topic theme 3

Qualitative theme	Participant Comment
3 Social activity with apps	
a) Female Parent	"There is a slight feeling of I won't say abandonment you don't feel like you are abandoned … The app I suppose it would be a great idea suppose there was someone I could ring to just give me a boost"
b) Female Parent	"… Ask how are you getting on say (from) the dietitian"
c) Female Parent	"If there like a boards thing – if there were people here and you recognised their name …"
d) Male Parent	"Keeping the communication going"
e) Male Parent	"People could put something down and some one would reply to it…"
f) Female Parent	"We know we are not the only ones, we are all in the same boat…. maybe for different reasons but we are all in the same boat"
g) Female Parent	"Share some personal information, you could give advice (to other attendees)"
h) Female Parent	"…I wouldn't mind but you see I am a bit nervous about that because sometimes they can become very personal. …Maybe I am being just a little paranoid I don't know I think I would be a bit nervous"
I) Female Parent	Private messages that no one else could see saying what goals they have achieved and what goals they want to achieve and what they have changed about their lifestyle"
j) Female Adolescent	"Well maybe it could be like Facebook but not like Facebook. But you could put up …you could say I have achieved that… but just a page with what you achieved and what goals you want to aim at and stuff like that"
k) Female Adolescent	"Well maybe if you wanted to text to people and say how you are and what goals do you want to achieve"

Table 4 Direct comments regarding safety and privacy

Qualitative theme	Participant Comment
4 Safety and privacy: privacy	
a) Female Adolescent	"I think it should have a password so only you can use it –So it's private…"
b) Female Adolescent	"…No one else could see what you are writing
c) Male Adolescent	**"**You should be able to choose if you want anonymous people or people who you are friends are with…"
d) Male Adolescent	"It could be like BBM (blackberry Messenger) but they wouldn't be able to see your weight or what you are doing -a tip could come on your screen and say what ever and them send it on and they would never have known it"
e) Male Adolescent	"Yes it would be good to have an email address and your own a password"
4 Safety and privacy: video diaries	
f) Female Parent	"Depends on who would have access to it"
g) Female Parent	"I don't think that they would want to …"(
h) Female Parent	"They have issues about being heavy so they are not wanting to…"
I) Female Parent	"I definitely would not"
j) Female Parent	"Yes I think I might – but it would have to monitored as well… I suppose in this day and age you have to be a bit cautious"
4 Safety and privacy: safety	
k) Female Parent	"I would have thought this one would be a safe one so why would we need to know what was on it"
4 Safety and privacy: bullying	
l) Female Adolescent	"You don't have to use your real name you have user name – you don't have to put your picture up if you did not want to you don't need to have your profile public or like private"

Table 5a direct comments regarding usability and design

Qualitative theme	Participant Comment
5a Usability and design	
a) Male Adolescent	"Things that would make you see everything something you would not have to go into a million different tabs Get to where you want to go to."
b) Female Adolescent	"Colour coded"
c) Male Adolescent	"User friendly "
d) Female Adolescent	"Bright colours stand out – if you are on a grey background it would be just boring"
5a Usability and design: personal preferences	
e) Female Adolescent	**"**If you could type in your height and weight… you would type in any allergies and they could give you a plan if there is anything you don't like you put it in…"
f) Female Adolescent	"It could say if you don't like brown bread or white bread you can eat what ever if you don't like fish then swap it for chicken"
g) Male Adolescent	"I think you should have breaks too cause some people might be pushing it too hard to do things
h) Female Adolescent	Most people would not want to do it at weekends… I know I would not. I would want to go out with my friends I would not be stopping when I am out with my friends and go for a jog– you could do it Monday to Friday or what every you wanted but you could still stop. I know for a fact I would not do it on a Friday for Saturday but I would do it on a Sunday – but you could choose "
I) Male Adolescent	"…You could have it manual or automatic" (for exercise
j) Male Adolescent	"… It would give you suggestions and you could take them on board or not (for exercise)"

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ARTICLE

High normal fasting glucose level in obese youth: a marker for insulin resistance and beta cell dysregulation

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Abstract
Aims/hypothesis A high but normal fasting plasma glucose level in adults is a risk factor for future development of type 2 diabetes mellitus and cardiovascular disease. We investigated whether normal fasting plasma glucose levels (<5.60 mmol/l) are associated with decreases in insulin sensitivity and beta cell function, as well as an adverse cardiovascular profile in obese youth.
Methods We performed a cross-sectional analysis in a multiethnic sample of 1,020 obese youth (614 girls and 406 boys; mean age 12.9 years [CI 95% 12.7–13.1], BMI *z* score 2.34 [CI 95% 2.31–2.38]) with normal fasting plasma glucose. All participants had a standard OGTT, with calculation of indices of insulin sensitivity and beta cell function. For the analysis, prepubertal and pubertal participants were stratified into quartiles of normal fasting plasma glucose.
Results We observed a significant increase in fasting insulin and AUC 2 h glucose across quartiles. Pronounced changes were observed in insulin sensitivity and secretion, particularly in the pubertal group. Moreover, the odds of presenting with impaired glucose tolerance increased by 4.5% with each 0.06 mmol/l increase in fasting plasma glucose. No significant differences in cardiovascular indices were seen across quartiles.
Conclusions/interpretation These data suggest that in obese youth, independent of age, BMI *z* score, sex, family history and ethnicity, insulin sensitivity and secretion decline when moving from low to high normal fasting plasma glucose. The simple measure of fasting plasma glucose could assist clinicians in identifying children for targeted diabetes screening and subsequent lifestyle management.

Keywords Beta cell dysregulation · Fasting plasma glucose · Insulin resistance · Obesity · Type 2 diabetes

Abbreviations

Δglucose	Mean change in glucose within the first 30 min of the OGTT
Δinsulin	Mean change in insulin within the first 30 min of the OGTT
CVD	Cardiovascular disease
DI	Disposition index
FPG	Fasting plasma glucose
IFG	Impaired fasting glucose
IGI	Insulinogenic index
IGT	Impaired glucose tolerance
NFPG	Normal fasting plasma glucose
WBISI	Whole body insulin sensitivity index

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Introduction

According to the latest estimates from the International Obesity Taskforce, at least 155 million school-age children

worldwide are overweight or obese [1]. Translated into clinical terms, this suggests that millions of children are now vulnerable to pathologies previously only seen in adults, such as type 2 diabetes mellitus, dyslipidaemia and hypertension. It is important that children at risk for such conditions be identified in order to implement effective management. Specifically, determining whether a child who is obese has a higher odds of presenting with risk factors known to lead to cardiometabolic disease is essential for the stratification of children to appropriate lifestyle interventions that improve the metabolic profile [2].

It has been demonstrated that impaired fasting glucose (IFG) is a clinical condition associated with a threefold increased risk of developing type 2 diabetes mellitus [3–7], and IFG status acts as a good marker of the acute insulin response and the disposition index (DI) [8, 9]. Although the established thresholds for defining IFG may be considered to be quite low, recent reports have suggested that fasting plasma glucose (FPG) within the normal range (NFPG) is a significant risk factor for future development of type 2 diabetes mellitus in adults [3–7]. Studies examining the association between NFPG and the risk of metabolic disease in children are sparse, although recent reports suggest that high NFPG levels constitute an independent risk factor for diabetes [10]. Thus, before fasting glucose reaches the diagnostic range for IFG, impairments in the regulation of glucose homeostasis might already exist. Studies investigating the association between NFPG and the risk of cardiovascular disease (CVD) are limited in adults [3, 11, 12] and even more sparse in children [10]. The aim of the present study was to investigate whether NFPG levels in a large multiracial sample of obese children and adolescents could act as a marker of metabolic and cardiovascular deterioration. It was hypothesised that in obese youth, as FPG rises within the normal range, the odds of presenting with decreased insulin sensitivity, beta cell dysregulation and cardiovascular disease profile would be greater.

Methods

Study population

We performed a cross-sectional study of metabolic and cardiovascular risks factors in 1,377 obese children and adolescents (BMI >95th percentile for age and sex) referred to the Yale Pediatric Obesity and Lipid Disorders Clinic from 2000 to 2008. Obese children and adolescents are referred to our clinic by local community paediatricians in the area of New Haven, CT. Eligibility for the study was determined by a comprehensive medical examination before enrolment. The physical examination included determination of the stage of puberty according to the criteria of Tanner. All participants underwent an OGTT at baseline, before starting any treatment or intervention. We excluded 272 children whose FPG was greater than or equal to 5.6 mmol/l and 85 children who had a previous history of impaired glucose tolerance, abnormal thyroid function or previous use of any medication known to affect glucose, blood pressure or lipid metabolism. In addition, information regarding a family history of type 2 diabetes mellitus was collected. The final sample included 1,020 children and adolescents with NFPG. The study protocol was approved by the institutional review board of the Yale University School of Medicine, and written parental consent and child assent were obtained before the study.

Testing procedures

A standard OGTT was performed in all children and adolescents to establish glucose tolerance status. Subjects were studied at the Hospital Research Unit at the Yale University School of Medicine at 08:00 hours, after a 10 h overnight fast. Children were advised to follow a meal plan that included >250 g of carbohydrate per day for 7 days before testing, and on the day before the OGTT they were advised to refrain from strenuous activity. Body weight, percentage body fat and BMI were measured using a Body Fat Analyzer (Tanita Corporation, Arlington Heights, IL, USA); and height was measured in triplicate with a wall-mounted stadiometer. Blood pressure was measured three times with a sphygmomanometer (model 01-752, American Diagnostics, Hauppauge, NY, USA) while the participants were seated, and the last two measurements were averaged for analysis. After the local application of a topical anaesthetic cream containing 2.5% lidocaine and 2.5% prilocaine, one antecubital intravenous catheter was inserted for blood sampling and was maintained patent by a saline drip. Two baseline samples were then obtained at −15 and 0 min for measurements of plasma glucose, insulin and a fasting lipid profile. Thereafter, the participant drank a flavoured glucose drink (Custom Laboratories, Baltimore, MD, USA) containing 1.75 g glucose/kg body weight, to a maximum of 75 g of glucose. Subsequent blood samples were obtained for measurement of glucose and insulin levels at 30, 60, 90, 120 and 180 min. Impaired glucose tolerance (IGT) and type 2 diabetes mellitus were defined according to American Diabetes Association guidelines [13].

Biochemical analyses

Plasma glucose was determined using the YSI 2700 Stat Analyzer (Yellow Springs Instruments, Yellow Springs, OH, USA). Plasma insulin was measured using RIA assays (Linco Research, St Charles, MO, USA) and lipid levels were measured with the use of an auto-analyser (model 747-200, Roche Hitachi, Indianapolis, IN, USA).

Calculations from the OGTT

Indices of insulin sensitivity The whole body insulin sensitivity index (WBISI) is a surrogate measure of insulin sensitivity, which we have previously described and validated against the euglycaemic–hyperinsulinaemic clamp in obese children and adolescents [14, 15]. The total AUC for glucose during OGTT ($AUC_{2h\ glucose}$) was calculated using the trapezoidal (trapezium) rule [16], and that number was then divided by 120 min to obtain an average level during OGTT.

Beta cell function The insulinogenic index (IGI), which represents early phase insulin secretion and is a commonly used surrogate index of beta cell function, was calculated from the OGTT data: IGI=Δinsulin (0–30 min) in μU/ml divided by the Δglucose (0–30 min) in mg/dl (to convert IGI to SI units [pmol/mmol], multiply by 125.01). The DI was calculated as the product of the IGI and the WBISI, based on the curvilinear relation of these OGTT-derived variables, previously described by our group in obese children and adolescents [17] (to convert DI to SI units [l^2/$mmol^2$], multiply by 324).

Statistical analyses For the purpose of investigating the association between normal fasting plasma glucose and metabolic and cardiovascular risk factors, our sample was stratified into quartiles of NFPG. Quartiles were chosen, rather than the continuous distribution of NFPG, to address the somewhat skewed distribution of NFPG and for ease of clinical interpretation. Sample characteristics such as age, pubertal stage, height, weight, BMI *z* score and percentage body fat were summarised and compared between the quartiles of NFPG using ANOVA. Post hoc pair-wise comparisons were made, adjusting the level of significance for multiple comparisons with the Bonferroni correction. Sex, family history of type 2 diabetes mellitus, race and pubertal status were compared using the χ^2 test.

Multiple linear regression was used to evaluate the difference between the quartiles of NFPG in prepubertal and pubertal participants for each of the metabolic and cardiovascular risk factors, adjusting for age, sex, ethnicity and BMI *z* score. Where appropriate, log transformations were used to normalise outcome variables with skewed distributions. Results are presented as least square means with 95% CIs, obtained from the multiple regression models. In a confirmatory analysis, NPFG was treated as a continuous variable in regression models assessing the presence of impaired insulin sensitivity and secretion or cardiovascular risks.

Logistic regression was also used to determine the probability of developing IGT/type 2 diabetes mellitus associated with each mmol/l increase in FPG. Logistic regression models were adjusted for age, sex, ethnicity, pubertal status and BMI *z* score. For both multiple and logistic regression, the models were also run using family history of type 2 diabetes mellitus; however, owing to a high number of missing values and very similar results, we excluded the variable. Results are presented as ORs with 95% CIs. Statistical significance in the multiple regression and logistic regression models was established with an alpha of 0.05, with appropriate corrections for multiple comparisons when required. Statistical analyses were performed with SAS (version 9.1; SAS Institute, Cary, NC, USA).

Results

Sample characteristics and fasting plasma glucose distribution by pubertal status

In total, 1,020 children and adolescents were included in the analyses. Of these, 60% were female, 37% were white, 33% were African-American and 30% were Hispanic. There were more pubertal children (844, 83%) in the cohort than prepubertal (176, 17%, p=0.04). The mean FPG for the full cohort was 5.00 mmol/l (range 3.42–5.54), and a significant difference (p=0.003) was observed between the mean FPG of prepubertal (4.95 mmol/l, 95% CI 4.90–5.00 mmol/l) and postpubertal children (5.03 mmol/l, 95% CI 5.00–5.05 mmol/l). A difference was also observed between the FPG distribution in prepubertal children and pubertal children (p=0.02). Figure 1 presents the distribution of FPG in our study sample divided by pubertal status. No statistical differences were seen between quartiles for those children with a positive family history of type 2 diabetes mellitus based on data available from 850 children (Table 1).

Clinical characteristics of the study cohort according to FPG quartiles

All children were stratified into quartiles (Q) of FPG (Q1 3.42–4.81 mmol/l; Q2 4.82–5.04 mmol/l; Q3 5.05–5.26 mmol/l; and Q4 5.27–5.54 mmol/l). No differences were seen in mean and 95% CIs for FPG between

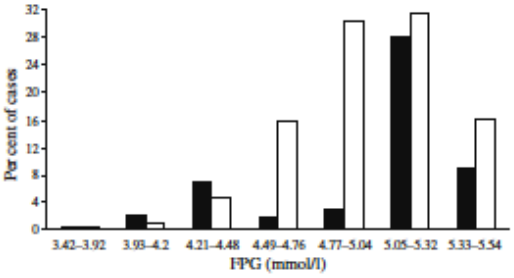


Fig. 1 Distribution of FPG throughout the normal range, stratified by pubertal status (p=0.02). Black bars, prepubertal children; white bars, pubertal children

Table 1 Clinical characteristics of the study cohort according to FPG quartile

Characteristic	Quartile 1 3.42–4.81 mmol/l (n=255)	Quartile 2 4.82–5.04 mmol/l (n=255)	Quartile 3 5.05–5.26 mmol/l (n=255)	Quartile 4 5.27–5.54 mmol/l (n=255)	p value[a]
Age (years)					
Prepubertal					
Mean	7.9	8.5	8.7	8.8	0.01[a]
95% CI	7.5–8.2	7.9–9.0	8.3–9.0	8.4–9.1	
Pubertal					
Mean	13.9	13.8	13.8	13.8	0.8
95% CI	13.6–14.3	13.5–14.1	13.5–14.1	13.5–14.1	
Sex (n, %)					
Male	77 (30)	103 (40)	107 (42)	119 (47)	<0.002[b]
Female	178 (70)	152 (60)	148 (58)	136 (63)	
Pubertal status (n, %)					
Prepubertal	57 (22)	46 (18)	43 (16.5)	33 (13)	0.03[c]
Postpubertal	198 (88)	209 (82)	212 (83.5)	222 (87)	0.03[c]
Ethnicity (n, %)					
White	116 (46)	89 (35)	101 (40)	91 (36)	0.1
African-American	85 (33)	87 (35)	79 (30)	88 (35)	0.1
Hispanic	54 (21)	79 (30)	75 (30)	76 (29)	0.1
+ve family hx T2DM					
Prepubertal	7 out of 43	13 out of 42	8 out of 39	7 out of 25	0.4
Postpubertal	37 out of 161	40 out of 172	50 out of 184	44 out of 184	0.8
Height (cm)					
Prepubertal					
Mean	134.9	140.1	137.8	141.6	0.02[d]
95% CI	131.8–138.1	136.9–143.4	134.6–141.1	138.9–144.4	
Pubertal					
Mean	160.4	160.6	161.4	163.8	0.001[d]
95% CI	158.9–161.8	159.2–1661.9	160.2–162.6	162.4–165.1	
Weight (kg)					
Prepubertal					
Mean	57.8	61.2	56.3	63.7	0.3
95% CI	52.4–63.2	55.0–67.4	51.8–60.7	58.6–68.9	
Pubertal					
Mean	92.1	91.9	96.1	63.7	0.04
95% CI	88.4–95.7	88.5–95.2	92.6–99.6	94.3–101.0	
BMI SDS					
Prepubertal					
Mean	2.62	2.46	2.49	2.56	0.3
95% CI	2.5–2.73	2.3–2.62	2.35–2.63	2.47–2.6	
Pubertal					
Mean	2.21	2.28	2.35	2.36	0.02[e]
95% CI	2.13–2.3	2.21–2.36	2.29–2.41	2.29–2.42	
Percentage body fat					
Prepubertal					
Mean	46.1	44.6	44.9	46.2	0.8
95% CI	42.5–49.8	42.5–47.6	42.1–47.6	42.8–49.7	
Pubertal					
Mean	44.3	44.6	45.6	44.4	0.5
95% CI	42.7–45.9	43.3–45.8	44.3–46.9	43.2–45.6	

Table 1 (continued)

Characteristic	Quartile 1 3.42–4.81 mmol/l (n=255)	Quartile 2 4.82–5.04 mmol/l (n=255)	Quartile 3 5.05–5.26 mmol/l (n=255)	Quartile 4 5.27–5.54 mmol/l (n=255)	p value[a]
IGT status (n, %)					
Prepubertal	5 (18)	4 (17)	6 (17)	4 (10)	>0.05[f]
FPG mean	4.49	4.92	5.14	5.40	
FPG 95% CI	4.31–4.67	4.83–5.00	5.06–5.23	5.29–5.52	
Pubertal	23 (82)	20 (83)	30 (83)	38 (90)	
FPG mean	4.59	4.96	5.16	5.41	
FPG 95% CI	4.48–4.69	4.92–4.99	5.14–5.19	5.38–5.44	

+ve family hx T2DM, positive family history of type 2 diabetes mellitus; BMI SDS, body mass index standard deviation score

[a] Post hoc pair-wise comparisons showed a significant difference between Q1 and Q3 (p=0.03) and between Q1 and Q4 (p=0.03)

[b] Post hoc pair-wise comparisons showed that there was a significantly greater proportion of girls to boys between Q1 and Q2 (p<0.001), Q1 and Q3 (p<0.001), Q1 and Q4 (p<0.001), Q2 and Q4 (p<0.05)

[c] Post hoc pair-wise comparisons showed that there was a significantly greater proportion of pubertal to prepubertal children between Q1 and Q3 (p=0.07) and Q1 and Q4 (p=0.005)

[d] Post hoc pair-wise comparisons showed a significant difference between Q1 and Q4 (p=0.04) for prepubertal children and between Q1 and Q4 (p=0.002) and Q2 and Q4 (p=0.02) for pubertal children

[e] Post hoc pair-wise comparisons showed a significant difference between Q1 and Q3 (p=0.05) and Q1 and Q4 (p=0.04) in pubertal children

[f] Post hoc pair-wise comparisons of prepubertal and pubertal children showed no difference between mean FPG values

prepubertal and pubertal children in each quartile (Q1 4.57 mmol/l [95% CI 4.50–4.63 mmol/l] and 4.60 mmol/l [95% CI 4.57–4.63 mmol/l]; Q2 4.94 mmol/l [95% CI 4.92–4.96 mmol/l] and 4.92 mmol/l [95% CI 4.91–4.93 mmol/l]; Q3 5.16 mmol/l [95% CI 5.13–5.18 mmol/l] and 5.14 mmol/l [95% CI 5.13–5.15 mmol/l]; and Q4 5.37 mmol/l [95% CI 5.35–5.41 mmol/l] and 5.39 mmol/l [95% CI 5.38–5.40 mmol/l]).

Table 1 provides the basic anthropometric data for the study cohort according to FPG quartiles. No significant differences were seen between the quartiles for race and percentage body fat. Significant differences were observed for sex, pubertal status, height, weight and BMI standard deviation score (pubertal children only).

Prevalence of IGT and type 2 diabetes mellitus across quartiles of FPG

After the OGTT, 128 children (12.4%) were diagnosed with IGT and two children were diagnosed with type 2 diabetes mellitus. Of those with IGT, 19 were prepubertal (14.8%); 83 (64.8%) were girls (seven prepubertal); 29 (22.7%) were African-American and 29 (22.7%) were Hispanic (Table 1). For the statistical analysis, the two participants with diabetes were included with those with IGT.

Insulin sensitivity and secretion indices across quartiles of FPG

In both pre- and pubertal groups we found an increase in fasting insulin across quartiles of NFPG (Fig. 2a, b). Notably, however, these increases were more pronounced in the pubertal group. The AUC for 2 h glucose increased progressively with rising NFPG in both pre- and pubertal groups (Fig. 2c, d). Insulin sensitivity (WBISI) decreased progressively as NFPG levels increased, independently of age, sex, ethnicity and BMI z score (Fig. 3a, b). These changes were, however, greater and more significant in the pubertal group (p<0.001). Despite an unchanged IGI in both groups, we found a decrease in the DI only in the pubertal group (p<0.001; Fig. 3e, f). Similarly, regression analyses using NFPG as a continuous variable agreed with our observations using quartiles of NFPG.

Cardiovascular indices according to FPG

No statistically significant differences in cardiovascular indices were seen across the quartiles of FPG (Table 2).

Risk of impaired glucose tolerance, insulin sensitivity and beta cell function

The odds of presenting with IGT/type 2 diabetes mellitus in Q3 and Q4 for NFPG vs Q1 and Q2 for prepubertal and pubertal children, respectively, was 1.07 (95% CI 0.33–3.58; p=0.8) and 1.64 (95% CI 1.06–2.52; p=0.002) Moreover, for the full cohort, each 0.06 mmol/l increase in FPG was associated with an increased odds of presenting with IGT/type 2 diabetes mellitus of 4.5% (OR 1.045, 95% CI 1.009–1.08; p=0.001).

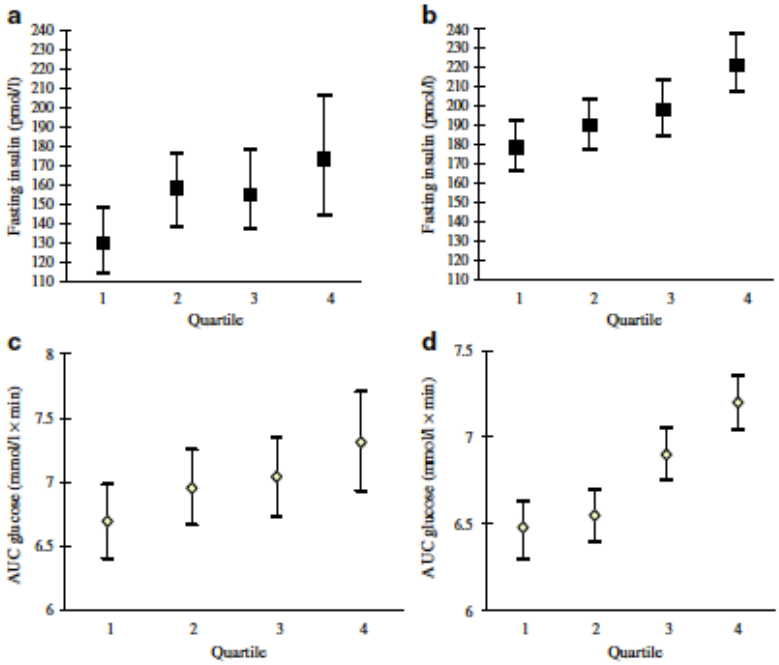


Fig. 2 A multiple linear regression approach was used to evaluate the effect of quartiles of FPG levels on each outcome of interest, adjusting for age, sex, pubertal status, ethnicity and BMI *z* score. Geometric means and surrounding CIs obtained from the models are presented. The statistical significance of differences in the outcomes by the four quartiles of fasting plasma glucose is expressed by the *p* value from the omnibus test. **a** Mean fasting insulin across quartiles of FPG in prepubertal children; $p=0.3$. **b** Mean fasting insulin across quartiles of FPG in pubertal children; $p<0.001$. **c** Mean AUC 2 h glucose across quartiles of FPG in prepubertal children; $p=0.04$. **d** Mean AUC 2 h glucose across quartiles of FPG in pubertal children; $p<0.001$. Significant post hoc pair-wise comparisons: (1) AUC 2 h glucose: Q1 vs Q3, $p<0.001$; Q1 vs Q4, $p<0.001$; Q2 vs Q3, $p<0.001$; Q2 vs Q4, $p<0.001$; Q3 vs Q4, $p=0.025$. (2) Fasting insulin in pubertal children: Q1 vs Q4, $p<0.001$; Q2 vs Q4, $p=0.008$

Discussion

In this cross-sectional study we evaluated whether rising NFPG levels were associated with pathophysiological cardiovascular and metabolic alterations. Our results indicated that in obese adolescents insulin sensitivity and beta cell function decrease significantly with increasing NFPG, independently of sex, ethnicity and BMI *z* score. In particular, we observed a significant increase in fasting plasma insulin and AUC 2 h glucose and a decrease in WBISI and DI across quartiles of NFPG. These changes were less pronounced in obese prepubertal children. As such, we found that despite having an NFPG, derangements in insulin sensitivity and beta cell function were still observed in obese youth. The fact that we observed significant decreases in insulin sensitivity and DI in the pubertal group is consistent with the higher prevalence rates of type 2 diabetes mellitus reported for this age group by the SEARCH study [18].

It should be noted that, although pubertal stage was not different across the quartiles, in the pubertal group the degree of obesity was significantly greater in quartile four than in quartile one ($p<0.02$). Therefore, although we adjusted for BMI *z* score, it is conceivable that the worsening in insulin resistance and secretion may have resulted from the greater severity of obesity in quartile four. Nevertheless, we argue that these changes are not a result of puberty, as we also observed a similar, although less pronounced, trend in the smaller group of prepubertal children.

Whether the rise in FPG reflects a derangement in insulin sensitivity and secretion or simply physiological variability, is an important issue that needs to be addressed. One should bear in mind that these results are obtained by using surrogate measures of insulin sensitivity and secretion obtained by OGTT as it would be difficult to evaluate insulin secretion and sensitivity in such a large sample of obese youth by using the gold standard euglycaemic–hyperinsulinaemic clamp for sensitivity and hyperglycae-

Table 2 Cardiovascular indices according to FPG quartile

Characteristic	Quartile 1 3.42–4.81 mmol/l *n*=255	Quartile 2 4.82–5.04 mmol/l *n*=255	Quartile 3 5.05–5.26 mmol/l *n*=255	Quartile 4 5.27–5.54 mmol/l *n*=255	*p* value[a]
Cholesterol[b]					
Prepubertal					
Mean	4.43	4.09	4.30	4.16	0.2
95% CI	4.12–4.74	3.80–4.74	4.01–4.60	3.78–4.53	
Pubertal					
Mean	4.11	4.23	3.99	4.09	0.1
95% CI	3.96–4.27	4.09–4.37	3.85–4.13	3.95–4.23	
LDL[b]					
Prepubertal					
Mean	2.69	2.44	2.48	2.50	0.5
95% CI	2.43–2.95	2.21–2.68	2.23–2.73	2.19–2.80	
Pubertal					
Mean	2.41	2.49	2.32	2.38	0.3
95% CI	2.28–2.54	2.37–2.62	2.20–2.43	2.26–2.50	
HDL[b]					
Prepubertal					
Mean	1.15	1.07	1.23	1.14	0.1
95% CI	1.06–1.24	0.99–1.16	1.14–1.32	1.03–1.25	
Pubertal					
Mean	1.09	1.12	1.13	1.16	0.6
95% CI	1.04–1.13	1.08–1.16	1.09–1.17	1.08–1.16	
Triacylglycerol[b]					
Prepubertal					
Mean	1.27	1.18	1.19	1.07	0.7
95% CI	1.03–1.51	0.96–1.40	0.96–1.42	0.78–1.35	
Pubertal					
Mean	1.35	1.39	1.24	1.30	0.8
95% CI	1.15–1.54	1.21–1.58	1.07–1.42	1.13–1.48	
Systolic BP (mmHg)					
Prepubertal					
Mean	116.9	114.6	115.4	115.1	0.8
95% CI	113.2–120.5	111.2–118.5	111.5–119.3	110.6–111.7	
Pubertal					
Mean	120.6	121.1	121.5	121.9	0.4
95% CI	118.9–122.4	119.5–122.8	119.8–123.1	120.3–123.5	
Diastolic BP (mmHg)					
Prepubertal					
Mean	67.5	68.5	67.7	66.4	0.8
95% CI	64.2–70.7	65.2–71.9	64.2–71.2	62.3–7.5	
Pubertal					
Mean	67.5	68.5	67.7	66.4	0.8
95% CI	68.5–71.4	69.9–72.6	70.0–72.7	69.9–72.6	

[a] *p* value obtained from a multiple linear regression, adjusted for age, sex, pubertal status, ethnicity and BMI *z* score

[b] Variables were $\log_e$-transformed for analysis

lower than expected acute insulin response subsequent to progressive insulin resistance, and a greater accumulation of visceral fat over time. Our group, using three serial OGTTs over a 3-year period in obese adolescents with normal glucose tolerance at baseline, observed remarkable stability in insulin sensitivity, beta cell function and DI [22]. By contrast, a decline in sensitivity, secretion and DI occurred in those obese adolescents that progressed to IGT. Thus, we consider that the described changes in insulin sensitivity and DI seen with rising NFPG in the present study are a true reflection of derangements in metabolism.

Our finding that high NFPG levels are correlated with reduced insulin sensitivity and beta cell dysfunction is supported by previous reports in adults that identified higher NFPG levels as an independent risk factor for impaired insulin secretion and type 2 diabetes mellitus in adults [6, 8]. Although our results are similar to those reported in adult studies, it is important to consider that the development of type 2 diabetes mellitus is a recent phenomenon observed in paediatrics. As such, investigations into the similarities and differences in pathological processes observed between children and adults are important, particularly if optimal therapy is to be implemented in childhood. A report from the Bogalusa Heart Study observed that adults who developed IGT or type 2 diabetes mellitus had higher glucose levels from childhood to adulthood compared with those adults who were normoglycaemic [12]. Also, a recent longitudinal study by Tirosh et al. [5] reported that high NFPG levels constituted an independent risk factor for the development of type 2 diabetes mellitus within a 10-year follow-up period. It is conceivable that some individuals may have an innate impaired beta cell capacity to compensate for insulin resistance. In fact, recent association studies, using powerful tools such as the genome-wide scan, produced a list of several genes associated with type 2 diabetes mellitus, the majority of which appear to be mainly implicated in beta cell function [23].

Nichols et al. observed a 6% increased risk of developing diabetes with each 0.06 mmol/l increase in FPG in a large group of adults [4]. Our results support the findings of this report, as our data indicated a 4.5% increased risk for presenting with IGT in adolescents with every 0.05 mmol/l increase in FPG. To our knowledge, this is the first investigation to report such data in a population of obese youth. Nichols and colleagues indicated that those with an FPG level between 5 and 5.56 mmol/l had a greater disease risk than those with an FPG<4.72 mmol/l, which further supports the findings of the current study.

The evaluation of beta cell function is important in clinical practice, although estimating this index can be time-consuming and somewhat impractical. A close relationship exists between FPG and beta cell function, and increasing levels of NFPG have been associated with a 32% decrease in the beta cell function of adults [7, 17]. Recently, DI has been shown to be predictive of the development of diabetes over 10 years [9]. The results of our investigation indicated that there is an increased risk of beta cell dysfunction with a decline in DI as NFPG increases.

Previous investigations suggest that FPG level is a risk marker for cardiovascular disease [3, 24]. Results from both the Diabetes Control and Complications Trial and the UK Prospective Diabetes Study Group support the use of appropriate glycaemic control for the prevention of atherosclerosis, and more recently these recommendations have been reasserted for youth with type 2 diabetes mellitus [25–27]. In addition, at 10-year follow up, longitudinal analyses observed the cardiovascular benefits of glucose control in adults with newly diagnosed type 2 diabetes mellitus [28]. Preventing atherosclerosis through better glucose control is a contentious topic, and in some epidemiologic studies the association between glucose control and cardiovascular disease has not been consistent [29–32]. Moreover, it has been shown that intensive glucose control in veterans with poorly controlled type 2 diabetes had no significant effect on the rates of major cardiovascular events, death or microvascular complications, with the exception of progression of albuminuria [33]. Few studies have investigated the relationship between normoglycaemia and risk factors for cardiovascular disease, although a report by Piche et al. [3] observed that higher triacylglycerol levels and reduced HDL-cholesterol were present in adults with high NFPG compared with those with lower NFPG. Contrary to these reports but in agreement with previous paediatric investigation, data from our study suggest that in children increases in FPG within the normal range are not associated with an increase in the cardiovascular risk profile [10]. This was also the case when the group was further divided by ethnicity (data not shown). The differences between adult and paediatric data may be ascribed to the younger age of participants included in our study and to their relatively short exposure to the hyperinsulinaemic environment. As such, it could be postulated that adverse effects in glucose metabolism may occur earlier than an adverse cardiovascular profile in children who are in the metabolically stressful state of obesity, which may require a longer period of exposure to hyperglycaemia and associated insulin resistance. If this is the case, a critical window of opportunity for effective treatment before the onset of cardiovascular damage might be available to clinicians when a child presents with a high NFPG.

Although the provision of a 'cut-off point' for normal glucose level was beyond the purpose of our study, the distribution of measured variables across quartiles of NFPG clearly shows that those children in quartile four display a higher risk for metabolic derangement. This suggests that FPG levels higher than 5.17 mmol/l might indicate a 'danger zone' for adolescents, given that after this level the

risk of IGT increases by 64% compared with those participants in the first three quartiles. As current paediatric definitions for IGT and IFG are based on adult studies, our data suggests that the 'cut-off point' for abnormality may be lower in children and adolescents, and thus represents a clinically meaningful observation.

As our sample was drawn from a clinical population in New Haven, these cross-sectional results may not be representative of the general paediatric population, although these children do reflect what general paediatricians are seeing in their daily practice. Similarly, our findings may not be applicable to those children of healthy weight. Furthermore, this study is a retrospective one and, as such, has all the limitations known to be associated with such investigations.

These data suggest that in prepubertal and pubertal obese youth insulin sensitivity declines when moving from low to high NFPG, independently of age, BMI, sex and ethnicity. Recent studies have demonstrated that lifestyle intervention can reduce risk factors for, and the incidence of, type 2 diabetes mellitus in children and adults and that those individuals presenting with prediabetes can convert back to normal glucose tolerance with appropriate lifestyle management [2, 34, 35]. Thus, FPG may be a useful measure for identifying children with higher odds of presenting with metabolic impairment and might be useful to identify those for whom subsequent targeted therapeutic lifestyle management would be most beneficial.

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Duality of interest The authors declare that there is no duality of interest associated with this manuscript.

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Long-term Results of an Obesity Program in an Ethnically Diverse Pediatric Population

WHAT'S KNOWN ON THIS SUBJECT: Long-term pediatric weight management studies have been predominantly carried out with affluent, white populations. Thus, evidence on successful management of childhood obesity is limited, especially in inner-city, ethnically diverse populations.

WHAT THIS STUDY ADDS: This randomized controlled trial bridges the gap in the pediatric obesity treatment literature by revealing a sustained treatment effect on anthropometric and metabolic markers after a family-based lifestyle intervention versus traditional clinical care in inner-city, ethnically diverse populations.

abstract

OBJECTIVE: To determine if beneficial effects of a weight-management program could be sustained for up to 24 months in a randomized trial in an ethnically diverse obese population.

PATIENTS AND METHODS: There were 209 obese children (BMI > 95th percentile), ages 8 to 16 of mixed ethnic backgrounds randomly assigned to the intensive lifestyle intervention or clinic control group. The control group received counseling every 6 months, and the intervention group received a family-based program, which included exercise, nutrition, and behavior modification. Lifestyle intervention sessions occurred twice weekly for the first 6 months, then twice monthly for the second 6 months; for the last 12 months there was no active intervention. There were 174 children who completed the 12 months of the randomized trial. Follow-up data were available for 76 of these children at 24 months. There were no statistical differences in dropout rates among ethnic groups or in any other aspects.

RESULTS: Treatment effect was sustained at 24 months in the intervention versus control group for BMI *z* score (−0.16 [95% confidence interval: −0.23 to −0.09]), BMI (−2.8 kg/m^2 [95% confidence interval: −4.0–1.6 kg/m^2]), percent body fat (−4.2% [95% confidence interval: −6.4% to −2.0%]), total body fat mass (−5.8 kg [95% confidence interval: −9.1 kg to −2.6 kg]), total cholesterol (−13.0 mg/dL [95% confidence interval: −21.7 mg/dL to −4.2 mg/dL]), low-density lipoprotein cholesterol (−10.4 mg/dL [95% confidence interval: −18.3 mg/dL to −2.4 mg/dL]), and homeostasis model assessment of insulin resistance (−2.05 [95% confidence interval: −2.48 to −1.75]).

CONCLUSIONS: This study, unprecedented because of the high degree of obesity and ethnically diverse backgrounds of children, reveals that benefits of an intensive lifestyle program can be sustained 12 months after completing the active intervention phase. *Pediatrics* 2011;127:402–410

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KEY WORDS

adolescents, children, BMI, obesity, behavior modification, exercise, insulin resistance

ABBREVIATION

HOMA-IR—homeostasis model assessment of insulin resistance

This trial has been registered at www.clinicaltrials.gov (identifier NCT00409422).

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Considering the high global prevalence of childhood obesity, it is surprising how little published evidence exists regarding successful treatment programs, especially in ethnic minorities and inner-city impoverished populations, which have the highest rates of childhood obesity. The first, a 2003 Cochrane review[1] on treatment of childhood obesity, referenced only 18 randomized controlled trials. Most of these studies had few subjects and targeted populations of white, educated, middle-class families. The Yale Bright Bodies Weight Management Program was developed to fill the unmet needs of obese, inner-city children who were primarily black and Hispanic. This family-based, intensive lifestyle program has been an ongoing treatment option available to overweight and obese children in the Greater New Haven area since 1998.

To evaluate the effectiveness of the Bright Bodies program, a 2-year, nonrandomized pilot study[2] was conducted that had lasting positive effects on body composition. Armed with this success, the next step was to design and implement an ambitious 12-month randomized controlled trial that compared the effects of Bright Bodies with outcomes of conventional clinical management in 209 children and adolescents. At the end of 12 months, virtually all anthropometric and metabolic parameters,[3] including increased insulin sensitivity and improved glucose tolerance,[4] favored the Bright Bodies groups over the clinic control group. The results were cited in the most recent Cochrane review and an evidence report prepared for the US Department of Health and Human Services as 1 of the best outcomes of intensive lifestyle interventions in children and adolescents.[5,6] However, it also was noted that longer-term follow-up of 2 years or more is critical to confirm maintenance of treatment effects and that such data are limited in the research literature on childhood obesity interventions.[5,6] Studies by Epstein et al[7–9] have included the longest observational study to date (10-year follow-up) of a behavioral intervention but were excluded by the Cochrane[6] and US Department of Health and Human Services[5] reports because they lacked comparison control groups. Consequently, in this article we will present the analysis and comparison of 24-month clinical and metabolic outcomes of the participants in the 2 groups in our randomized clinical trial that completed the 12 month extension phase of that study.

METHODS

Participants

Eligibility criteria, recruitment, and enrollment of participants in the randomized clinical trial were reported in detail elsewhere.[3] Subjects were recruited from the Yale Pediatric Obesity Clinic by clinicians who were coinvestigators. Major inclusion criteria included English-speaking, 8- to 16-year-old children with a BMI ≥ 95th percentile.[10] Exclusion criteria included serious medical conditions that would preclude participation in the program, use of medications that may cause significant weight gain/loss, or involvement in a coexisting weight management program. Participants randomly assigned to the control group were offered participation in the weight management program after 12 months, but only 1 family elected to do so. The rest were encouraged to continue with standard clinic appointments every 6 months and return for a final 24-month outcome measurement at clinic. The study was approved by the Yale Human Investigation Committee, and written informed assent and consent were obtained from participants and parents.

Study Design

The study was designed to be a 12-month parallel-group, randomized controlled trial with a 12-month extension phase. Recruitment occurred between May 2002 and September. 2004; 12-month follow-up ended in September 2005, and 24-month follow-up ended in September 2006. Participants were randomly assigned 2:1 by using a permuted block design to the weight management or clinic control group by the same coinvestigators who recruited the subjects. Random assignments were generated by computer and concealed by the study statistician (Dr Dziura). Initially, a second randomization (1:1) occurred within the weight management group to investigate types of diet intervention children received (ie, structured meal plan versus better food choices). However, randomization to the structured meal plan group was discontinued because of an 83% dropout rate at 6 months. After completion of the initial 12 months of the study, the weight management group participants were referred back to the Yale Pediatric Obesity Clinic for 6-month clinic appointments and received no additional intensive lifestyle intervention during the extension phase. The control group continued to attend 6-month clinic appointments for the last year.

Study Groups

Bright Bodies Weight Management Group

During the intervention phase of the program, participants randomly assigned to the Bright Bodies group attended the program at a nearby school twice a week for 6 months and then every other week for an additional 6 months. This setting was chosen with respect to the limited transportation options of the socioeconomically diverse families. The program consisted of exercise twice (50 minutes each)

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and nutrition/behavior modification once (40 minutes each) per week, described in detail previously.[3] Parents did not participate in the exercise component. Parents attended classes of nutrition-related topics, but did not attend behavior-modification-related topics with their child (they alternately attended their own parent class). Nutrition and behavior modification topics were based on the Smart Moves Workbook, a curriculum designed for overweight and obese children and written by 1 of the authors (Ms Savoye). Sample topics in the behavior modification component included "Ready, Set, Goal!," "Risky Business: Identifying High-risk Situations," "Mirror, Mirror on the Wall," "Bullies, Teasers, and Other Annoying People," and "Oops I Slipped: Understanding a Relapse." Techniques included self-awareness, goal-setting, stimulus control, coping-skills training, and cognitive behavior strategies. Behavior modification classes were facilitated by the registered dietitian or social worker. Parent classes included topics that reflected the challenges parents verbalized. These classes emphasized the importance of the parents' role in modeling healthy behavior change.

The nutrition education component of the program used a nondiet approach that emphasized low-fat, nutrient-dense foods of moderate portions. Topics included "Determining Portion Sizes," "Better Food Choices: A NonDiet Approach," "Making Sense of a Food Label," and "Bag It! Pros to Bringing Lunch to School." A favorite nutrition topic for parents and children alike was "Recipes Dear to the Heart," which includes a recipe for collard greens that has been trimmed of calories and fat. The topic also involves sharing traditional family recipes and working together as a team to modify it to be healthier. This topic is an example of how the program was tailored to inner-city, ethnically diverse populations. In addition, the dietitian was bilingual (Spanish) for parents who needed additional explanation of nutrition concepts.

The exercise component of the program was facilitated by exercise physiologists. Each class consisted of a warm-up, high-intensity aerobic exercise, and cool down. The high-intensity exercise consisted of a variety of children games, obstacle courses, basketball, flag football, sprinting games, and sport drills. The objective of the high intensity exercise was to sustain 65% to 80% of the age-adjusted maximal heart rate for the duration of the exercise. Participants were also encouraged to exercise 3 additional days at home per week and to decrease sedentary behaviors. The minimum activity that each participant completed was 100 minutes per week (2 50-minute sessions) for the first 6 months and 100 minutes twice per month for the last 6 months.

After completing 1 year of the program, participants were encouraged to stay active and apply the knowledge gained during the program when making food choices (nondiet approach) throughout the next year. They were referred back to the Yale Pediatric Obesity Clinic for follow-up where end of study assessments were made at 24 months.

Control Group

The control group participants were followed in the Yale Pediatric Obesity Clinic every 6 months and received general diet and exercise counseling (~30 minutes) by dietitians and physicians along with brief psychosocial counseling by a social worker (~30 minutes). At 24 months, the participants were asked to return for end-of-study assessments.

Outcomes

Outcome measures for 24 months were obtained at the Yale Pediatric Obesity Clinic with the same scale and instruments that were used in all subjects in both groups for the 24 months of the study. Outcome measures included weight (kg), height (cm), BMI (kg/m^2), percent body fat (%), total body fat (kg), blood pressure (mm Hg), lipid profile (total, high-density lipoprotein and low-density lipoprotein cholesterol, and triglycerides in mg/dL), fasting plasma glucose (mg/dL), fasting insulin (μIU/mL), and homeostasis model assessment of insulin resistance (HOMA-IR).

Weight was measured (participants in socks, no shoes, wearing light gown) to the nearest 0.1 kg using a medical weight scale (CN20, Detecto; Webb City, MO). Height was measured with a stadiometer (Harpenden; Cambridge, MD), calibrated in 0.1-cm intervals. BMI was calculated as weight in kg divided by height in meters squared. Percent body fat was obtained by a body fat analyzer (TBF 300, Tanita Corporation, Arlington Heights, IL). Total body fat was calculated by multiplying percent body fat by actual weight in kg. Blood pressure was measured automatically with a sphygmomanometer (01-752, American Diagnostics; Hauppauge, NY) 3 times after participants sat still for 5 minutes; second and third measurements were averaged for outcome.

Blood samples were obtained after a 10-hour overnight fast. Plasma glucose levels were measured with a chemistry analyzer (YSI 2700 STAT Analyzer, Yellow Springs Instruments; Yellow Springs, OH), and plasma insulin levels were measured by radiommunoassay (Linco Laboratories, St Charles, MO). Plasma lipid levels were measured with an autoanalyzer (747-200, Roche-Hitachi; Indianapolis, IN). HOMA-IR was calculated from fasting plasma glucose and insulin as follows: fasting plasma insulin (in μIU/mL) + fasting plasma glucose (in mmol/L)/22.5.[11]

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TABLE 1 Baseline Characteristics of Children Randomly Assigned to Weight Management and Control Group

	All Randomly Assigned Participants			Completers at 24 Mo		
	Weight Management Group ($n = 105$)	Control Group ($n = 69$)	*P*	Weight Management Group ($n = 45$)	Control Group ($n = 31$)	*P*
Race/ethnic group, *n* (%)						
Non-Hispanic White	40 (38.1)	24 (34.8)	.89	16 (35.6)	14 (45.2)	.42
Non-Hispanic Black	40 (38.1)	27 (39.1)		16 (35.6)	12 (38.7)	
Hispanic	25 (23.8)	18 (26.1)		13 (28.9)	5 (16.1)	
Gender, *n* (%)						
Female	58 (55.2)	47 (68.1)	.09	23 (51.1)	22 (71.0)	.08
Male	47 (44.8)	22 (31.9)		22 (48.9)	9 (29.0)	
Age, y	12.0 (2.5)	12.5 (2.3)	.19	12.0 (2.2)	12.2 (2.3)	.71
Weight, kg	87.0 (25.1)	91.2 (23.3)	.27	87.6 (20.8)	90.4 (23.1)	.58
Height, cm	155.0 (11.6)	157.7 (11.6)	.15	156.1 (10.0)	157.2 (11.5)	.67
BMI	35.7 (7.5)	36.2 (6.2)	.68	35.6 (6.4)	36.1 (5.3)	.75
BMI *z* score	2.47 (0.34)	2.48 (0.27)	.80	2.47 (0.34)	2.49 (0.26)	.72
Body fat, %	47.0 (8.7)	45.8 (7.2)	.37	46.9 (7.8)	46.2 (7.1)	.72
Body fat mass, kg	42.1 (18.1)	42.4 (14.9)	.91	41.5 (13.4)	42.6 (16.3)	.76
Blood pressure, mm Hg						
Systolic	123 (13.6)	122 (14.0)	.74	123 (15.4)	122 (15.4)	.70
Diastolic	66 (9.5)	67 (11.1)	.66	64 (9.3)	62 (9.7)	.47
Cholesterol, mg/dL						
Total	167 (34.5)	158 (33.5)	.07	167 (34.6)	165 (34.9)	.80
HDL	44 (10.8)	43 (16.5)	.78	42 (10.0)	43 (21.8)	.81
LDL	98 (33.4)	92 (28.0)	.16	98 (30.8)	96 (29.2)	.72
Triglycerides*	104 (1.8)	101 (1.6)	.79	112 (1.8)	112 (1.7)	.99
Fasting glucose	92 (8.3)	89 (8.5)	.09	92 (6.9)	90 (7.4)	.17
Fasting insulin*	23 (1.8)	24 (1.7)	.48	23.5 (1.62)	24.3 (1.55)	.76
HOMA-IR*	5.07 (1.87)	5.23 (1.7)	.74	5.34 (1.64)	5.30 (1.61)	.95

Data are presented as mean (SD) unless otherwise indicated. HDL indicates high-density lipoprotein; LDL, low-density lipoprotein.
* Data are presented as geometric means with geometric SDs.

Sample Size and Statistical Analysis

Group comparisons were made on the basis of the intent-to-treat principle, whereby all subjects were analyzed in the group to which they were randomly assigned. Baseline characteristics were compared by using *t* tests for continuous variables and χ^2 tests for nominal variables. Mixed model repeated measures analysis incorporating all available data was used to examine treatment differences in outcomes over time. In these models we assume missing data are missing at random, ie, missing values may depend on observed but not unobserved data.[12] The models included adjustment for baseline outcome, treatment assignment, time (6, 12, and 24 months), and a treatment by time interaction as fixed effects. The correlation of repeated measures was modeled using an unstructured covariance pattern whereby the correlation between alternative time-lags was allowed to vary. Log transformations were used for positively skewed variables. Mean changes from baseline and 95% confidence intervals derived from the mixed models are presented.

Before analysis, missing data patterns were evaluated using simple graphical and tabular methods. The pattern of missing data was the result of dropout where those missing an outcome at a time point had missing outcomes at all subsequent times. However, the missing levels of the outcomes were not related to observed previous levels of the outcomes or any baseline covariates for both treatment groups. For instance, those who dropped out had similar BMI profiles compared with those who did not drop out (data not shown). In addition, Pattern Mixture models, including dropout as a covariate, were used to examine the potential influence of dropout on outcome measures.[13] No effect by dropout was found on estimates of treatment, time, and treatment by time interaction, which means that the estimates have little dependency on a subject's completion of the study. Therefore, results of the pattern mixture models are not shown. All analysis was performed using SAS 9.1 (SAS Institute, Inc, Cary, NC), with statistical significance set at $P < .05$ using 2-sided tests.

RESULTS

Participants

As seen in Table 1, treatment groups were similar with regard to baseline characteristics. Dropouts were similar to completers with the exception of baseline diastolic blood pressure (Ta-

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TABLE 2 Baseline Characteristics of Children Who Dropped Out at Any Time Point and Nondropouts at All Time Points (Completed 24-Mo. Assessment)

	Nondropouts ($n = 76$)	Dropouts ($n = 98$)	P
Race/ethnic group, *n* (%)			
Non-Hispanic White	30 (39.5)	34 (34.7)	.81
Non-Hispanic Black	28 (36.8)	39 (39.8)	
Hispanic	18 (23.7)	25 (25.5)	
Gender, *n* (%)			
Female	45 (59.2)	60 (61.2)	.79
Male	31 (40.8)	38 (38.8)	
Age, y	12.1 (2.3)	12.2 (2.6)	.73
Weight, kg	88.7 (21.7)	88.6 (26.5)	.97
Height, cm	156.6 (10.6)	155.7 (12.4)	.63
BMI	35.8 (6.0)	36.0 (7.8)	.84
BMI *z* score	2.48 (0.31)	2.47 (0.32)	.91
Body fat, %	46.6 (7.5)	46.5 (8.6)	.91
Body fat mass, kg	42.0 (14.5)	42.4 (18.6)	.87
Blood pressure, mm Hg			
Systolic	123 (15.3)	122 (12.3)	.92
Diastolic	63 (9.4)	69 (10.1)	.0004
Cholesterol, mg/dL			
Total	166 (34.5)	162 (34.3)	.44
HDL	43 (15.8)	44 (11.1)	.58
LDL	97 (30.0)	95 (32.7)	.60
Triglycerides[a]	112 (1.7)	96 (1.8)	.08
Fasting glucose	91 (7.2)	90 (9.3)	.47
Fasting insulin[a]	24 (1.6)	22 (1.9)	.47
HOMA-IR[a]	5.33 (1.62)	4.99 (1.94)	.45

Data are presented as mean (SD) unless otherwise indicated. HDL indicates high-density lipoprotein; LDL, low-density lipoprotein.
[a] Data are presented as geometric means with geometric SDs.

ble 2). Of the 75 weight management group participants reported on at 12 months, 45 were available for outcome measures at 24 months (60% retention rate). Of the 44 control group participants reported on at 12 months, 31 were available for outcome measures at 24 months (70% retention rate).

As shown in the consort diagram in Fig 1, the most common reasons for dropping out were similar in both groups (moved with no forwarding address and not interested). The 1 control group participant who decided to receive the intervention at 12 months was considered a "drop out" from the control group. The category "lost to follow-up" includes those who could not be contacted because their telephone was out of service or the caregivers did not respond to telephone calls/letters. The percentage of participants lost to follow-up was similar in both groups.

Effects of Treatment

Anthropometric

Changes from baseline in BMI, BMI *z* score, and body fat are shown in Table 3. The treatment effect between the weight management group and control group for BMI *z* score (see Fig2) and BMI was sustained at 24 months ($P < .0001$). Likewise, both body fat percent ($P < .0001$) and total body fat ($P < .0001$) also resulted in a sustained treatment effect favoring the weight management group.

Metabolic

As with the 6- and 12-month data, there was no statistical significance in treatment effect for systolic and diastolic blood pressures at 24 months ($P = .81$ and $P = .38$, respectively). Treatment effect for total cholesterol ($P = .004$) and low-density-lipoprotein cholesterol ($P = .01$) were both significant, whereas high-density lipoprotein was not ($P = .18$). Although fasting triglycerides and glucose also were not significantly different, fasting insulin was lowered, and HOMA-IR (see Fig 2) markedly improved with the Bright Bodies intervention ($P = .0001$).

DISCUSSION

The results of this study reveal that the beneficial effects of the Bright Bodies weight management program on body weight, body composition, plasma lipids and insulin, and insulin sensitivity were sustained in comparison to the clinic control group for 24 months, although the lifestyle intervention phase of the study ended after 12 months. Although the differences in outcomes between the 2 treatment groups were greater at 12 than at 24 months, the 24-month results indicate that education, behavior modification, and exercise training had a long-lasting effect on the food choices and physical activity in these ethnically diverse, primarily low-income, obese children. These results are particularly noteworthy because no randomized control trials in pediatrics have demonstrated long-term maintenance of positive outcomes beyond the first 6 to 12 months in disadvantaged, inner-city populations.

Although the attrition rate was high at 24 months, the dropout rates were similar in both treatment groups, according to baseline characteristics. Likewise, follow-up outcomes were similar among those who dropped out compared with those who completed the 24-month follow-up. In addition, in analyzing the 24-month data, statistical measures were employed to evaluate the effect of attrition, including comparing results in completers-only with results from methods that are more robust to missing data (ie, mixed models and pattern-mixture models). Conclusions were unaltered by these various approaches.

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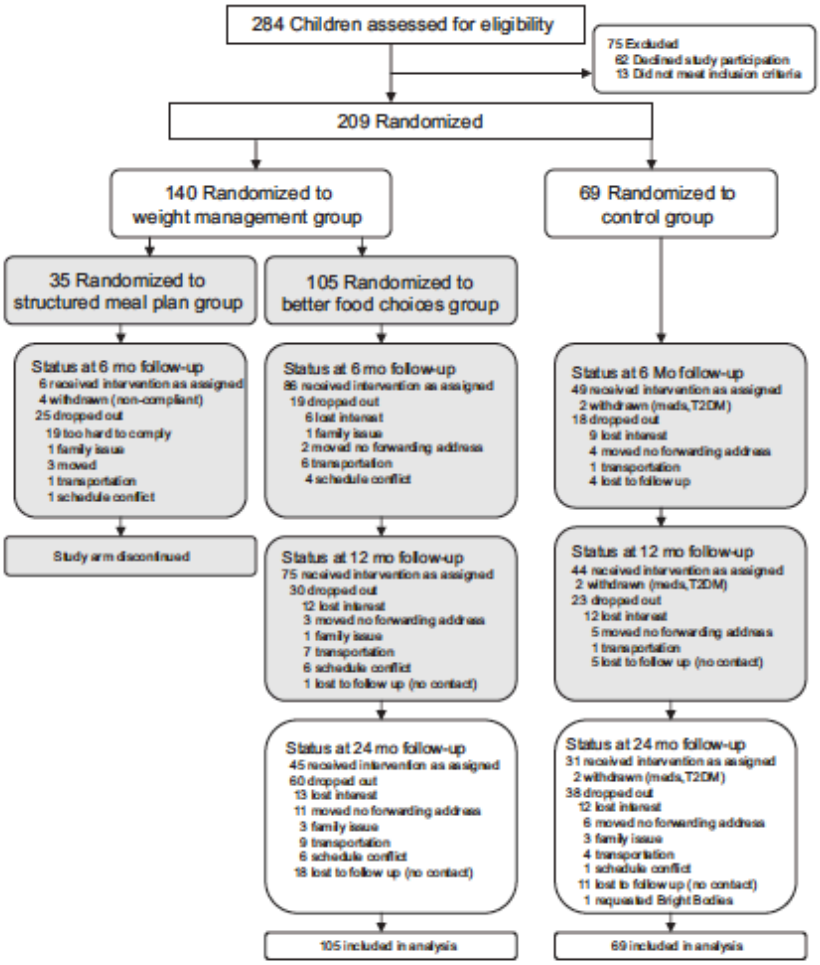


FIGURE 1
Flowchart for enrollment, randomization, and follow-up of study participants.

Of the 54 lifestyle modification trials included in the most recent Cochrane review,[6] only 16 studies reported 24-month data, only 4 studies[14–17] had baseline BMIs as high as our subjects, only 1 study targeted non-white populations,[17] and all had high drop-out rates. Moreover, in the 1 study that targeted black youth,[17] the treatment effect was lost by 24 months.[18] One aim of future studies is to determine whether the program would be equally effective if the subjects met only once versus twice per week. This reduced program "dose" might ease the burden on the families and perhaps lower the overall drop-out rate for these interventions. Although annual program satisfaction questionnaires indicated that twice-weekly sessions were not a burden, we should not ignore that 6% of the overall intervention group dropouts were because of schedule conflicts.

In addition to reduction of adiposity, other major clinical benefits of this program were the continuous improvements of HOMA-IR and fasting insulin because severe insulin resistance is so common in prediabetic obese youth.[19] Indeed, during the initial 12-month randomized phase of this

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TABLE 3 Changes From Baseline in Body Composition, Cardiovascular, and Insulin Sensitivity Parameters for Weight Management and Control Groups at 6, 12, and 24 Mo

Outcome	Month	Weight Management Group, Mean (95% CI)	Control Group, Mean (95% CI)	Treatment Effect (Intervention-Control), Mean (95% CI)	Between-Group *P*
Weight, kg	6	−2.4 (−4.0 to −0.8)	4.6 (2.5 to 6.8)	−7.0 (−9.8 to −4.3)	<.0001[a]
	12	0.3 (−1.4 to 2.0)	8.3 (6.1 to 10.6)	−8.0 (−10.9 to −5.2)	<.0001[a]
	24	5.9 (4.0 to 7.9)	12.0 (9.5 to 14.6)	−6.1 (−9.3 to −2.9)	.0002[a]
Height, cm	6	2.5 (1.8 to 3.2)	2.0 (1.1 to 3.0)	0.4 (−0.7 to 1.6)	.45
	12	4.5 (3.8 to 5.2)	3.5 (2.5 to 4.4)	1.0 (−0.2 to 2.2)	.10
	24	7.7 (6.8 to 8.6)	6.4 (5.2 to 7.5)	1.3 (−0.1 to 2.8)	.07
BMI	6	−2.1 (−2.7 to −1.5)	0.9 (0.1 to 1.7)	−3.0 (−4.0 to −2.0)	<.0001[a]
	12	−1.8 (−2.4 to −1.1)	1.9 (1.1 to 2.8)	−3.7 (−4.8 to −2.6)	<.0001[a]
	24	−0.9 (−1.7 to −0.1)	1.9 (0.9 to 2.9)	−2.8 (−4.0 to −1.6)	<.0001[a]
BMI *z* score	6	−0.16 (−0.20 to −0.13)	0.01 (−0.04 to 0.05)	−0.18 (−0.24 to −0.12)	<.0001[a]
	12	−0.21 (−0.25 to −0.17)	0.01 (−0.04 to 0.07)	−0.23 (−0.29 to −0.16)	<.0001[a]
	24	−0.20 (−0.25 to −0.16)	−0.05 (−0.10 to 0.01)	−0.16 (−0.23 to −0.09)	<.0001[a]
Body fat, %	6	−2.7 (−3.9 to −1.6)	2.1 (0.6 to 3.6)	−4.9 (−6.7 to −3.0)	<.0001[a]
	12	−3.9 (−5.1 to −2.8)	2.1 (0.6 to 3.6)	−6.0 (−7.9 to −4.1)	<.0001[a]
	24	−3.6 (−4.9 to −2.3)	0.6 (−1.2 to 2.3)	−4.2 (−6.4 to −2.0)	.0002[a]
Body fat mass, kg	6	−3.6 (−5.3 to −1.9)	4.3 (2.1 to 6.6)	−7.9 (−10.8 to −5.1)	<.0001[a]
	12	−3.7 (−5.4 to −1.9)	5.7 (3.4 to 8.1)	−9.4 (−12.3 to −6.5)	<.0001[a]
	24	−0.6 (−2.6 to 1.4)	5.2 (2.6 to 7.8)	−5.8 (−9.1 to −2.6)	.0005[a]
Blood pressure, mm Hg systolic	6	−1.5 (−3.7 to 0.7)	0.4 (−2.6 to 3.3)	−1.9 (−5.6 to 1.8)	.31
	12	−1.3 (−3.7 to 1.1)	−0.3 (−3.4 to 2.8)	−1.0 (−4.9 to 2.9)	.62
	24	−2.5 (−5.5 to 0.5)	−1.9 (−5.8 to 1.9)	−0.6 (−5.5 to 4.3)	.81
Blood pressure, mm Hg diastolic	6	−2.2 (−4.3 to −0.2)	1.4 (−1.3 to 4.1)	−3.6 (−7.0 to −0.3)	.04[a]
	12	1.3 (−0.9 to 3.5)	2.3 (−0.5 to 5.2)	−1.1 (−4.6 to 2.5)	.56
	24	0.8 (−1.9 to 3.5)	2.8 (−0.7 to 6.3)	−2.0 (−6.4 to 2.4)	.38
Cholesterol, mg/dL total	6	−4.2 (−8.5 to 0.1)	4.6 (−1.2 to 10.3)	−8.8 (−15.9 to −1.6)	.02[a]
	12	−4.7 (−9.2 to −0.1)	6.5 (0.5 to 12.4)	−11.2 (−18.7 to −3.6)	.004[a]
	24	−8.0 (−13.5 to −2.4)	5.0 (−1.8 to 11.8)	−13.0 (−21.7 to −4.2)	.004[a]
Cholesterol, mg/dL HDL	6	1.5 (−0.4 to 3.4)	−0.7 (−3.2 to 1.9)	2.2 (−1.0 to 5.4)	.18
	12	2.0 (0.1 to 4.0)	0.3 (−2.3 to 2.9)	1.8 (−1.5 to 5.0)	.29
	24	3.7 (1.5 to 5.9)	1.3 (−1.6 to 4.1)	2.5 (−1.1 to 6.1)	.18
Cholesterol, mg/dL LDL	6	−0.7 (−4.5 to 3.2)	5.3 (0.2 to 10.4)	−6.0 (−12.3 to 0.4)	.07
	12	0.3 (−3.8 to 4.3)	5.8 (0.5 to 11.1)	−5.5 (−12.2 to 1.2)	.11
	24	−4.4 (−9.5 to 0.6)	5.9 (−0.2 to 12.1)	−10.4 (−18.3 to −2.4)	.01[a]
Triglycerides, mg/dL[b]	6	−12.5 (−17.2 to −6.3)	−0.7 (−10.3 to 12.9)	−11.8 (−20.8 to −0.5)	.04[a]
	12	−14.5 (−18.9 to −8.6)	−4.2 (−13.1 to 8.7)	−10.4 (−19.5 to 0.6)	.06
	24	−17.0 (−21.2 to −10.6)	−6.6 (−15.7 to 7.4)	−10.4 (−20.2 to 1.3)	.07
Fasting glucose, mg/dL	6	−1.9 (−3.4 to −0.3)	−0.9 (−2.9 to 1.1)	−0.9 (−3.5 to 1.6)	.46
	12	−2.4 (−4.1 to −0.8)	−1.1 (−3.2 to 1.1)	−1.4 (−4.1 to 1.3)	.32
	24	−1.7 (−3.9 to 0.4)	−1.5 (−4.1 to 1.2)	−0.3 (−3.7 to 3.1)	.87
Fasting insulin, μIU/mL[b]	6	−4.5 (−5.2 to −3.5)	1.3 (−1.9 to 6.1)	−5.8 (−7.9 to −4.5)	.0001[a]
	12	−4.6 (−5.3 to −3.4)	3.4 (−0.7 to 9.6)	−8.0 (−10.0 to −6.9)	<.0001[a]
	24	−4.7 (−5.5 to −3.2)	4.5 (−0.8 to 13.2)	−9.2 (−11.0 to −7.5)	.0001[a]
HOMA-IR[b]	6	−1.04 (−1.18 to −0.80)	0.26 (−0.46 to 1.38)	−1.29 (−1.78 to −1.02)	.0001[a]
	12	−1.07 (−1.21 to −0.82)	0.72 (−0.21 to 2.16)	−1.78 (−2.24 to −1.60)	<.0001[a]
	24	−1.07 (−1.23 to −0.76)	0.98 (−0.22 to 3.03)	−2.05 (−2.48 to −1.75)	.0001[a]

Data are presented as mean (SD) unless otherwise indicated. HDL indicates high-density lipoprotein; LDL, low-density lipoprotein.

[a] Statistically significant.

[b] Data are presented as geometric means with geometric SDs.

study, oral glucose tolerance tests were performed in a subgroup of 13 Bright Bodies and 10 control subjects. After 12 months of the Bright Bodies program, the 3 subjects with prediabetes reverted to normal glucose tolerance, whereas 4 subjects in the control groups progressed from normal to impaired glucose tolerance.[4] In response to these promising results, a larger study in which oral glucose tolerance test outcomes in prediabetic, obese children randomly assigned to Bright Bodies or clinic control group interventions are compared is currently under way. Additional longitudinal investigation of the clinical significance of reductions in adiposity and HOMA-IR reveals that there is a relationship to these 2 biological markers. In fact, Morrison et al[28] found HOMA-IR and insulin levels at 9 to 10 years old to predict increased BMI and impaired fasting glucose and type 2 diabetes

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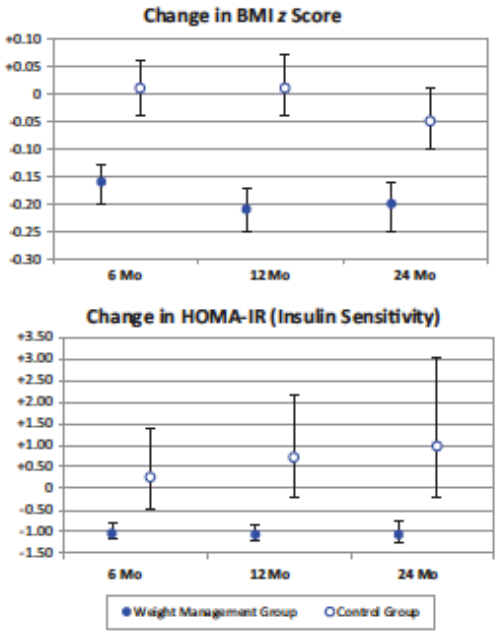


FIGURE 2

Changes from 6, 12, and 24 months are from baseline. At 6 months (weight management group, $n = 86$; control group, $n = 49$) $P < .0001$ for BMI z score, and $P = .0001$ for HOMA-IR; at 12 months (weight management, $n = 75$; control group, $n = 44$) $P < .0001$ for BMI z score and HOMA-IR; and at 24 months (weight management group, $n = 45$; control group, $n = 31$) $P < .0001$ for BMI z score, and $P = .0001$ for HOMA-IR.

mellitus, respectively, 10 years later. In addition, the Bogalusa Heart Study has recently confirmed that adiposity and HOMA-IR are interrelated.[21]

Programs that include increased activity and behavior modification have traditionally resulted in more improvements in childhood obesity.[6] During the development of the program, the major goal was to provide the child and parent with tools to empower them to make better decisions that would promote a healthier lifestyle. Leaving the families "to their own devices" between 12 and 24 months with the result of a sustained treatment effect highly suggests that the child and parent adopted healthier behaviors. However, in an attempt to avoid characteristics of dieting, we deliberately avoided requesting food diaries, which resulted in a lack of measurement in diet change. Similarly, we lack measurement of activity change because we did not collect activity records when requesting an additional 3 days of activity.

The lack of psychosocial measures should also be included as a limitation of this study. Lastly, a study of this nature would not be complete without mention of the cost-effectiveness and cost/benefit of the weight management program verses clinical treatment approach. Such an analysis has been completed on the 12-month data (Nowicka P, Price G, Vipin S, Shaw M, Mercado J, Tamborlane WV, Savoye M, unpublished data, 2010).

CONCLUSION

The Bright Bodies intensive lifestyle modification program has demonstrated sustained treatment effects up to 24 months when compared with a standard clinical care. Although the attrition rate was high, this study is unique and, more importantly, unprecedented in that we targeted ethnically diverse children with very high BMIs. This gives us hope that behavior change is possible, even in the most challenging populations. Although global focus is shifting to the prevention of childhood obesity, it is equally urgent to pursue treatment models that are effective for those who need immediate treatment.

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Ethnic differences in lipoprotein subclasses in obese adolescents: importance of liver and intraabdominal fat accretion[1–4]

Ebe D'Adamo, Veronika Northrup, Ram Weiss, Nicola Santoro, Bridget Pierpont, Mary Savoye, Grace O'Malley, and Sonia Caprio

ABSTRACT

Background: Recently, the deleterious metabolic effects of visceral fat [visceral adipose tissue (VAT)] deposition were challenged, and liver fat emerged as having a key independent role in the modulation of cardiometabolic risk factors.

Objective: We explored the relation between liver fat content and VAT in 3 ethnic groups and evaluated whether the ethnic differences in the distributions of lipoprotein concentrations and sizes were associated with the hepatic fat fraction (HFF), VAT, or both.

Design: In a multiethnic group of 33 white, 33 African American, and 33 Hispanic obese adolescents with normal glucose tolerance, we measured VAT and HFF by using magnetic resonance imaging. Fasting lipoprotein particle number and size were measured by using nuclear magnetic resonance spectroscopy. To assess the association between VAT and HFF, we categorized VAT into tertiles.

Results: In each ethnic group, HFF values increased between successive tertiles of VAT. After multivariate adjustment and in comparison with the 2 other groups, African Americans showed lower triglyceride ($P = 0.001$) and higher HDL ($P = 0.03$) concentrations, lower concentrations of total ($P = 0.007$), large ($P = 0.005$), and medium ($P < 0.0001$) VLDL, but higher concentrations of large HDL particles ($P = 0.01$) and larger HDL ($P = 0.005$). In multivariate linear models, independent of ethnicity, VAT was a significant predictor for large HDL ($P = 0.003$) and total small LDL ($P = 0.001$) concentrations, whereas HFF significantly predicted large VLDL ($P = 0.03$) concentrations.

Conclusion: Liver fat accretion, independent of VAT, may play a role in the ethnic differences seen in large VLDL particles. This trial was registered at clinicaltrials.gov as NCT00536250. *Am J Clin Nutr* 2010;92:500–8.

INTRODUCTION

The metabolic effects of obesity and insulin resistance are different in African American children and adults than in whites and Hispanics (1, 2). Despite higher prevalence rates of obesity in African American adolescents, metabolic syndrome features are significantly less pronounced in African American adolescents than in their white and Hispanic counterparts (3, 4). Indeed, the concentrations of triglycerides and HDL cholesterol have been shown to be lower and higher, respectively, across all age groups in African Americans than in whites and Hispanics (5, 6).

Although the factors responsible for these interracial differences are not completely known, it is likely that genetic differences could explain some of the interethnic differences in the lipoprotein profile. In particular, it was shown that polymorphisms in the lipoprotein lipase gene (*LPL*) (7) and hepatic lipase gene (*LIPC*) (8) strongly contribute to the different lipid profiles among different ethnicities.

Along with genetic factors, fat distribution may also play a pivotal role in determining the different lipoprotein phenotypes among different ethnic groups. In fact, the lower concentrations of triglycerides have been attributed to the lower accumulation of visceral adipose tissue (VAT) (6) that are typically seen in African Americans.

Few studies in adults have taken into account the potential contribution of liver fat content to alterations in the lipid profile (9, 10). The liver plays a critical role in glucose and lipid metabolism (11). The measurement of the hepatic fat fraction (HFF) by either nuclear magnetic resonance (NMR) spectroscopy or magnetic resonance imaging (MRI) has provided a unique opportunity to understand the role of hepatic fat in the complex clustering of cardiometabolic risk factors. Numerous studies indicate that, independent of overall adiposity, VAT is related to HFF in adults (12). A recent study by Guerrero et al (13) showed that liver fat accumulation in a large group of adults was closely linked to visceral adiposity, regardless of ethnicity. Given that the 2 fat depots, VAT and HFF, tend to track together, it is conceivable that VAT itself may not be deleterious, and liver fat may ultimately be more closely related to dyslipidemia and insulin resistance. Indeed, a recent study by Fabbrini et al (14) contradicted

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the prevailing dogma that VAT has deleterious metabolic effects in adults.

With the use of fast gradient MRI to assess liver fat content, multislice MR imaging to measure abdominal fat, and proton NMR spectroscopy for quantifying lipoprotein subclasses, in our current study we explored *1*) the relation between liver fat content and abdominal fat distribution in African American, white, and Hispanic obese adolescents with normal glucose tolerance (NGT) and *2*) investigated whether liver fat content or intrabdominal fat content or both were associated with ethnic differences in the distributions of lipoprotein concentrations and sizes.

SUBJECTS AND METHODS

Study population

Thirty-three (33) white (12 men and 21 women), 33 Hispanic (13 men and 20 women), and 33 African American (10 men and 23 women) obese [body mass index (BMI) >95th percentile] adolescents with NGT [2 h glucose <7.7 mmol/L (140 mg/dL)] were recruited from the Yale Pediatric Obesity Clinic. Detailed medical and family histories were obtained from all subjects, and physical examinations were performed. The Tanner stage of pubertal development was obtained. Participants were eligible if they were not taking any medications known to affect glucose metabolism or abdominal fat distribution.

The study protocol was approved by the institutional review board of the Yale University School of Medicine, and written parental consent and child assent were obtained before the study.

Metabolic studies

Before the assessment of the lipoprotein profile and glucose tolerance status, all subjects were instructed by a registered dietitian to follow a diet of ≈2000 calories (15% protein, 30% fat, and 55% carbohydrate) and to refrain from strenuous physical activity for 1 wk. Thus, all 3 groups were exposed to a similar diet and exercise regimen to minimize the potential effects of dietary factors and physical activity on lipid and glucose metabolism.

Oral-glucose-tolerance test

A standard oral glucose tolerance test was performed in all adolescents to establish glucose tolerance status. Subjects were studied at the Yale Clinical Center Investigation at 0800 after a 10-h overnight fast as previously reported (3). Body weight and percentage body fat were measured with a body fat analyzer (Tanita Corporation, Arlington Heights, IL), and height was measured in triplicate with a wall-mounted stadiometer. Blood pressure was measured 3 times with a sphygmomanometer (model 01–752; American Diagnostics, Hauppauge, NY) while the subjects were seated, and the 2 last measurements were averaged for analysis. NGT was defined according to the guidelines of the American Diabetes Association (15).

Indexes of insulin sensitivity

Insulin sensitivity was assessed by the whole-body insulin sensitivity index (WBISI) derived from the glucose and insulin concentrations during the oral-glucose-tolerance test (16). WBISI was validated against the hyperinsulinemic-euglycemic clamp studies in obese children and adolescents (17).

Lipoprotein analyses

Fasting plasma samples were obtained to determine lipoprotein particle concentrations and sizes. The analyses were conducted with a 400-MHz proton NMR analyzer at Liposcience (Raleigh, NC). The methodology has been described in detail (18). In brief, each lipoprotein subclass concentration was measured by the amplitudes of the characteristic lipid-methyl group NMR signals that they emit (19). The intensity of each signal was proportional to the quantity of the subclass, which was reported in particle concentration units (in nmol/L for VLDL and LDL and μmol/L for HDL cholesterol). VLDL, LDL, and HDL cholesterol were separated into 10 subclass categories: large VLDL (including chylomicrons) (>60 nm), medium VLDL (35–60 nm), small VLDL (27–35 nm), intermediate-density lipoprotein (IDL) (23–27 nm), large LDL (21.2–23 nm), medium-small LDL (19.8–21.2 nm), very small LDL (18–19.8 nm), large HDL (8.8–13 nm), medium HDL (8.2–8.8nm), and small HDL (7.3–8.2 nm). Average particle sizes were computed as the sum of the diameter of each subclass multiplied by its relative mass percentage as estimated from the amplitude of its methyl NMR signal.

Imaging studies

Abdominal MRI and total body composition (dual-energy X-ray absorptiometry)

Multislice abdominal MRI studies were performed with a Siemens Sonata 1.5 T system (Siemens, Malvern, PA) as previously described (20). Total body composition was measured by dual-energy X-ray absorptiometry with a Hologic scanner (Hologic, Boston, MA).

Fast MRI: liver fat content

Measurement of liver fat content was performed by MRI by using the 2-point Dixon (2PD) method modified by Fishbein et al (21) on the basis of phase-shift imaging, where HFF was calculated from the signal difference between the vectors that resulted from in-phase and out-of-phase signals. With the use of the MRIcro software program (version 1.40; Atlanta, GA), 5 regions of interest were drawn on each image, and the mean pixel signal-intensity level was recorded. The HFF was calculated in duplicate from the mean pixel signal-intensity (*S*) data by using the formula:

$$[(S_{in} - S_{out})/(2 \times S_{in})] \times 100 \qquad (1)$$

The presence or absence of steatosis was measured by a threshold value for HFF of 5.5% (>2.5 SD above the mean of our control subjects). This cutoff is supported by the results from a large study that applied a more quantitative measure of hepatic fat content by using 1H magnetic resonance spectroscopy of which the 95th percentile of hepatic fat content was 5.5% (22, 23).

Validation of fast MRI

We validated the modified 2PD method against ^{1}H-NMR in 34 lean and obese adolescents and observed a very strong correlation between the 2 methods ($r = 0.954$, $P < 0.0001$) (24).

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To assess its repeatability (test and retest reliability), measurements were obtained (within the same day) in 12 subjects. The within-subject SD for HFF was 1.9%. This degree of reproducibility was well within the boundaries necessary to make this a viable method to assess the relation between HFF and metabolic outcomes. Kim et al (24) observed that a 2PD HFF cutoff of 3.6% provided good sensitivity (80%) and specificity (87%) compared with a ^{1}H magnetic resonance spectroscopy reference. Comparisons between the 2PD method and histologic determination of fatty liver have been made, albeit only in adults. In 38 patients who were undergoing biopsies for a variety of liver diseases, Fishbein et al (25) observed a highly significant correlation between liver histology and MRI determination of HFF, particularly with macrovesicular steatosis ($r = 0.920$, $P < 0.001$).

Biochemical analyses

Plasma glucose concentrations were measured with the YSI 2700 Stat Analyzer (Yellow Springs Instruments, Yellow Springs, OH), and lipid concentrations were measured with an Auto-Analyzer (model 747–200; Roche-Hitachi, Indianapolis, IN). Plasma insulin and total adiponectin concentrations were measured with a double-antibody radioimmunoassay (Millipore, Billerica, MA); liver enzymes were measured by using automated kinetic enzymatic assays (Yale Clinical Chemistry Laboratory, Yale New Haven Hospital, New Haven, CT).

Statistical analyses

The first aim of the study was an exploratory one in which we anticipated from previously published studies and our own clinical experience that the proportion of children with the lowest or highest tertiles of visceral fat would be different within each ethnic group although there would be an approximately normal distribution of visceral fat in the group of children studied. For the second aim, with 33 subjects per ethnic group, we proposed that we would have an 80% power to detect an R^2 in the range of 5.6–6.4% attributed to either visceral fat or liver fat by using an F test with a significant level (α) of 0.05. The variables tested would be adjusted for an additional 4 independent variables (race, BMI z score, percentage body fat, and WBISI) with an R^2 that ranged between 0.15 and 0.25. The final multiple regression models for aim 2 were powered at 80% to have a total R^2 in the range between 0.21 and 0.31.

Anthropometric variables were compared among ethnicities by using analysis of variance. Adjusted comparisons were performed by using general linear models adjusted for age, sex, BMI Z score, and percentage body fat. Post hoc pairwise comparisons were made by using Tukey's test. Sex and pubertal status (Tanner stage II compared with stages III–IV) were compared by using chi-square statistics.

For the purpose of exploring the association between VAT and HFF, we categorized visceral fat depot (in cm^2) into tertiles. The data are presented as box plots of HFF by tertiles of VAT within each race (smallest observation, lower quartile, median, upper quartile, and largest observation). For each ethnicity, the nonparametric Kruskal-Wallis test was used to compare the distribution of HFF across the tertiles of VAT. Wilcoxon's rank sum test was used to conduct post hoc pairwise comparisons between tertiles with the level of α adjusted with the Bonferroni correction ($0.05/3 \approx 0.02$). The potential moderating effect of ethnicity on the association between HFF and VAT was explored with linear regression analysis that included an interaction between the tertiles of VAT and ethnicity adjusted for age, sex, BMI z score, and percentage body fat.

Multiple linear regression models, adjusted for age, sex, BMI z score and percentage body fat, were used to evaluate ethnic differences in plasma lipids and lipoprotein concentrations and sizes. Results are presented as adjusted means (±SEs) obtained from the multiple regression models.

For multiple linear regression analyses, adjusted for age, sex, BMI z score, percentage body fat, and WBSI, we used a stepwise approach to first evaluate ethnic differences in large VLDL concentrations and VLDL sizes, small LDL concentrations and LDL sizes, large HDL concentrations and HDL sizes (model a) and then tested the independent effects of VAT (model b) and HFF (model c) on the outcomes over and above those attributable to ethnicity. Model d tested whether VAT or HFF or both significantly predicted the outcomes of interest. A final adjusted model for each outcome was selected among the models a, b, c, and d on the basis of the R^2 statistic and the relative contribution of VAT or HFF or both at $\alpha < 0.05$. Because multicollinearity was a potential pitfall in the regression models, we used a tolerance <0.20 or variance inflation factor ≥ 5 to indicate a problem with multicollinearity.

Where appropriate, log transformations were used to normalize outcome variables with skewed distributions. Statistical significance in the multiple regression models was established with $\alpha = 0.05$ with appropriate corrections for multiple comparisons when required. Statistical analyses were performed with SAS software (version 9.1; SAS Institute Inc, Cary, NC).

RESULTS

Demographic and anthropometric characteristics

There were more girls (64.6%) than boys (35.4%) in our population, and the mean age of participants was 14.6 ± 2.7 y. The sex and age distribution were similar in all 3 ethnic groups. The pubertal stage of development did not differ among ethnicities ($P = 0.5$). On average, BMI and BMI z scores were significantly higher in African Americans than in white and Hispanic groups (P for BMI = 0.007, P for BMI z score = 0.005) (**Table 1**).

Percentage body fat was greater in African American youths that in either white ($P = 0.006$) or Hispanic ($P = 0.007$) groups. Despite the greater level of overall adiposity in African American adolescents, significant differences emerged in the distribution of body fat. VAT was significantly lower in African Americans than in Hispanics ($P < 0.0001$) and whites ($P < 0.0001$), whereas subcutaneous fat was comparable among ethnicities. HFF results paralleled the findings of the VAT. HFF was significantly lower in African Americans than in white ($P = 0.001$) and Hispanic ($P = 0.01$) youths.

Metabolic characteristics

Fasting glucose, 2-h glucose, and adiponectin concentrations were not significantly different between ethnicities ($P > 0.05$). Likewise, no significant ethnic differences were shown for

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TABLE 1
Clinical characteristics of study groups[1]

Characteristic	White	Hispanic	African American	*P*
No. of subjects (M:F)	12:21	13:20	10:23	0.7[2]
Age (y)	14.9 ± 2.2	14.1 ± 2.7	14.7 ± 2.9	0.6[3]
Tanner stage [*n* (%)]				
II	20 (60.6)	20 (60.6)	16 (48.5)	0.5[2]
III–IV	13 (39.4)	13 (39.4)	17 (51.5)	
BMI (kg/m^2)	35.1 ± 7.6^{a,b}	33.0 ± 6.3^{a}	38.2 ± 5.7^{b}	0.007[3]
BMI *z* score	2.2 ± 0.4^{a}	2.1 ± 0.5^{a}	2.5 ± 0.4^{b}	0.005[3]
Waist circumference (cm)	107.4 ± 13.2	101.9 ± 15.6	110.9 ± 12.5	0.04[3,4]
Body fat (%)	41.9 ± 6.6^{a}	42.0 ± 7.4^{a}	47.2 ± 5.7^{b}	0.002[3]
Body fat distribution				
Abdominal (cm^2)				
VAT	73.9 ± 3.7^{a}	69.6 ± 3.7^{a}	43.4 ± 4.0^{b}	<0.0001[5]
SAT	538.1 ± 18.40	539.5 ± 18.5	533.3 ± 20.3	0.9[5]
Liver				
Hepatic fat fraction (%)[4]	12.8 ± 1.7^{a}	10.2 ± 1.7^{a}	1.43 ± 1.9^{b}	0.001[5]
Metabolic variable				
Fasting glucose (mg/dL)[4]	92.9 ± 1.4	91.8 ± 1.4	95.9 ± 1.5	0.2[5]
2-h glucose (mg/dL)[4]	113.7 ± 3.0	110.8 ± 3.0	115.2 ± 3.4	0.7[5]
Fasting insulin (μU/mL)[4]	30.2 ± 3.0	34.3 ± 2.9	36.9 ± 3.3	0.3[5]
Adiponectin (μg/mL)[4]	8.52 ± 0.8	8.0 ± 0.8	8.8 ± 0.9	0.8[5]
WBISI[4]	1.8 ± 0.1	1.7 ± 0.1	1.8 ± 0.2	0.5[5]
Liver enzymes (U/L)				
ALT[4]	32.0 ± 4.2^{a}	30.5 ± 4.2^{a,b}	13.9 ± 4.7^{b}	0.006[5]
AST[4]	27.6 ± 2.2^{a}	25.9 ± 2.2^{a,b}	18.7 ± 2.5^{b}	0.008[5]
Systolic blood pressure (mm Hg)	119.0 ± 1.8	116.6 ± 1.8	116.3 ± 1.9	0.5[5]
Diastolic blood pressure (mm Hg)	70.9 ± 1.4	70.6 ± 1.4	68.9 ± 1.5	0.6[5]

[1] VAT, visceral fat; SAT, subcutaneous fat; WBISI, whole-body insulin-sensitivity index; ALT, alanine transaminase; AST, aspartate aminotransferase. Values are numbers of subjects (percentages) for the Tanner index, means ± SDs for ANOVA, and means ± SEMs or geometric means ± SEMs for the general linear model. Values not sharing a common superscript letter were significantly different on the basis of Tukey's test in the post hoc analyses for only significant omnibus tests.
[2] Derived by chi-square analysis.
[3] Derived by ANOVA.
[4] Log transformed for analysis.
[5] Derived by general linear model analysis adjusted for age, sex, BMI *z* score, and body fat.

fasting insulin and insulin sensitivity (WBISI). Alanine transaminase and aspartate aminotransferase concentrations were significantly lower ($P = 0.006$ and $P = 0.008$, respectively) in African Americans than in both white and Hispanic adolescents. Systolic and diastolic blood pressures were comparable among the ethnicities ($P > 0.05$).

Ethnic differences in the relation between visceral fat depot and hepatic fat content

After we observed that visceral and liver fat significantly varied by ethnicity, we examined the effect of increasing amounts of VAT on the accumulation of fat in the liver within each ethnic group. As shown in **Figure 1**, in white and Hispanic adolescents, HFF values significantly increased across tertiles of VAT ($P = 0.002$ and $P = 0.004$, respectively). In African American obese youths, HFF showed an increasing trend across the tertiles of VAT ($P = 0.105$).

Post hoc pairwise comparisons of HFF distributions between specific tertiles of VAT showed that HFF significantly increased with increasing of VAT in whites and Hispanics, whereas this was not observed in African Americans. The nonsignificant association between rising levels of visceral fat and hepatic fat in the African American group could be due to the small sample size, which may preclude any significant difference. The interaction between ethnicity and tertiles of visceral fat was not significant ($P = 0.830$), which indicated that the rate of increase in HFF across the tertiles of VAT did not significantly differ between the 3 ethnic groups.

Ethnic differences in plasma lipids and lipoprotein concentrations and sizes

Plasma lipids

Lower concentrations of triglycerides ($P = 0.001$) and higher concentrations of HDL cholesterol ($P = 0.03$) were observed in African American youths than in the other 2 groups. No ethnic differences were detected for concentrations of total cholesterol ($P = 0.8$) and LDL cholesterol ($P = 0.8$) (**Table 2**).

VLDL particle concentrations

After adjustment for age, sex, BMI *Z* score, and percentage body fat, concentrations of total VLDL ($P = 0.007$), large VLDL ($P = 0.005$), and medium VLDL ($P < 0.0001$) were consistently lower for African Americans than for the other 2 ethnicities.

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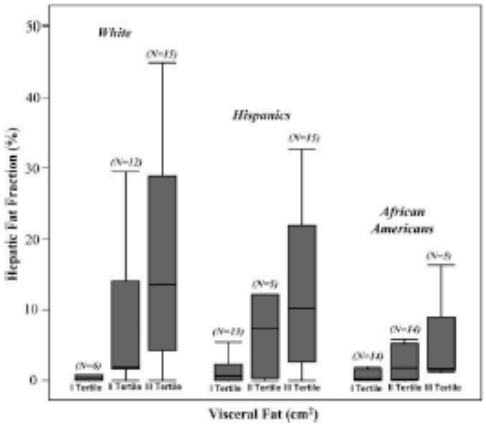


FIGURE 1. Hepatic fat fraction (HFF) across visceral fat tertiles in obese adolescents of different ethnicity. Data are presented as box plots of HFF by tertiles of visceral adipose tissue (VAT) within each race (smallest observation, lower quartile, median, upper quartile, and largest observation). For each ethnicity, the nonparametric Kruskal-Wallis test was used to compare the distribution of HFF across tertiles of VAT (whites: $P = 0.002$; Hispanics: $P = 0.004$; African Americans: $P = 0.1$). Wilcoxon's rank sum test was used to conduct post hoc pairwise comparisons between tertiles. Critical $\alpha < 0.02$ (Bonferroni correction).

IDL particle concentrations

No ethnic differences were detected for the IDL particle concentrations among groups ($P = 0.8$).

LDL particle concentrations

Comparable distributions of concentrations for total LDL ($P = 0.5$), large LDL ($P = 0.8$), total small LDL ($P = 0.3$), medium-small LDL ($P = 0.4$), and very small LDL ($P = 0.3$) were observed across different ethnicities. It should be noted that all 3 groups had higher concentrations of small LDL particles than of large LDL particles. This overproduction of small LDL may be related to the ambient degree of insulin resistance, which was similar across the groups.

HDL particle concentrations

African American obese adolescents had significantly higher concentrations of large HDL particles than did white obese adolescents ($P = 0.01$). Concentrations of total HDL ($P = 0.3$), medium HDL ($P = 0.9$), and small HDL ($P = 0.3$) did not substantially vary by ethnicity.

Particle sizes

With regard to overall sizes of the lipoproteins, no significant ethnic differences were observed for VLDL particle sizes ($P = 0.2$) or LDL particle sizes ($P = 0.2$). African Americans had

TABLE 2
Plasma lipids and lipoprotein profiles in children of different ethnicity[1]

	White ($n = 33$)	Hispanic ($n = 33$)	African American ($n = 33$)	P (adjusted)[2]
Plasma lipids (mg/dL)				
Total cholesterol[3]	159.5 ± 6.2	161.0 ± 6.2	155.5 ± 6.8	0.8
LDL cholesterol[3]	92.5 ± 5.5	97.2 ± 5.5	92.4 ± 6.0	0.8
HDL cholesterol[3]	42.1 ± 1.7	42.4 ± 1.7	48.2 ± 1.8	0.03
Triglycerides[4]	107.8 ± 8.8[a]	95.8 ± 8.9[a]	67.5 ± 9.85[b]	0.001
VLDL particles (nmol/L)				
Total VLDL and chylomicrons[3]	53.7 ± 3.5[a]	53.8 ± 3.5[a]	38.9 ± 3.8[b]	0.007
Large VLDL and chylomicrons[4]	3.9 ± 0.7[a]	2.8 ± 0.7[a]	1.3 ± 0.8[b]	0.005
Medium VLDL[4]	17.4 ± 1.9[a]	15.7 ± 1.9[a]	8.8 ± 2.1[b]	<0.0001
Small VLDL[3]	33.9 ± 2.3	35.2 ± 2.3	29.4 ± 2.5	0.2
IDL particles (nmol/L)[4]	37.3 ± 5.4	34.3 ± 5.5	33.0 ± 5.7	0.8
LDL particles (nmol/L)				
Total[3]	1013.0 ± 48.4	975.3 ± 48.7	933.4 ± 53.4	0.5
Large[3]	314.7 ± 26.5	321.9 ± 26.3	338.8 ± 28.8	0.8
Total small[3]	672.4 ± 46.2	623.1 ± 46.5	560.6 ± 50.9	0.3
Medium-small[3]	136.8 ± 9.1	128.0 ± 9.2	118.3 ± 10.0	0.4
Very small[3]	535.6 ± 37.8	495.0 ± 38.1	442.3 ± 41.7	0.3
HDL particles (μmol/L)				
Total[3]	26.6 ± 0.7	25.1 ± 0.7	25.7 ± 0.7	0.3
Large[3]	4.1 ± 0.4[a]	4.3 ± 0.4[a,b]	5.6 ± 0.4[b]	0.01
Medium[4]	3.6 ± 0.5	3.4 ± 0.5	2.7 ± 0.6	0.9
Small[3]	18.9 ± 0.6	17.6 ± 0.6	17.8 ± 0.7	0.3
VLDL size (nm)[3]	52.9 ± 1.8	52.4 ± 1.8	48.4 ± 2.0	0.2
LDL size (nm)[3]	20.8 ± 0.1	20.9 ± 0.1	21.0 ± 0.1	0.2
HDL size (nm)[3]	8.7 ± 0.06[a]	8.7 ± 0.06[a,b]	8.9 ± 0.06[b]	0.005

[1] IDL, intermediate-density lipoprotein. Values not sharing a common superscript letter were significantly different in the post hoc analyses with Tukey's test.

[2] Derived by general linear model analysis adjusted for age, sex, BMI z score, and body fat followed by post hoc pairwise comparisons for only significant omnibus tests.

[3] Values are means ± SEMs for nontransformed outcomes.

[4] Values are geometric means ± SEMs for log-transformed outcomes.

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significantly larger HDL particle sizes ($P = 0.005$) than did the other 2 groups.

Effect of hepatic fat content [HFF (%)] and visceral fat [VAT (cm^2)] on ethnic differences in the proatherogenic profile

Large VLDL particle concentrations and VLDL sizes

After adjustment for age, sex, insulin sensitivity, BMI *z* score, total body fat, VAT, and HFF, multiple regression analyses indicated that the distribution of large VLDL concentrations was not influenced by ethnicity ($P > 0.05$) (model d; **Table 3**). Although we observed a trend for VAT in model b ($P = 0.08$), when HFF was added in model d, the predictive value of VAT became not significant ($P = 0.29$) (Table 3). Therefore, model d was selected as the final adjusted model (Table 3), which accounted for 40% of the variability in the distribution of large VLDL concentrations, with the dependent variable predicted by HFF ($P = 0.03$) significantly and independently of VAT ($P = 0.29$).

There were no ethnic differences in VLDL sizes in the adjusted multiple regression models c and d in **Table 4** ($P > 0.05$ for ethnic comparisons). HFF ($P = 0.02$) was a significant independent predictor (model c for VLDL size; Table 4). However, when VAT was added in model d, the predictive value of HFF decreased ($P = 0.07$), whereas that the predictive value of VAT remained not significant ($P = 0.32$). Therefore, model d was selected as the final model for VLDL size ($R^2 = 0.265$).

Small LDL particle concentrations and LDL sizes

The distributions of total small LDL concentrations and LDL sizes did not vary by ethnicity ($P > 0.05$ for comparisons between ethnicities). The final model was chosen to be model d, with VAT as the significant independent predictor, and explained 30% of the variability in the concentrations of total small LDL ($R^2 = 0.296$) (Table 3).

VAT was also a significant predictor of LDL size (model b for LDL size; Table 4). However when VAT and HFF were added to the regression (model d), VAT became less significant ($P = 0.08$), whereas HFF remained not significant ($P = 0.43$). Therefore, the final model for LDL size was model d in Table 4.

HDL particle concentrations and HDL sizes

Ethnic differences in large HDL concentrations and sizes were significantly explained by VAT. The final model was chosen to be model b with VAT as the significant independent predictor. This model explained 33% of the variability in the distribution of HDL concentrations (model b; Table 3) and 36% of variability in the

TABLE 3
Effect of hepatic fat content, visceral fat, and ethnicity on large VLDL, total small LDL, and large HDL particle concentrations[1]

	Dependent variable								
	Log large VLDL (nmol/L)			Total small LDL (nmol/L)			Large HDL (μmol/L)		
Independent variable	R^2	β (SEE)	*P*	R^2	β (SEE)	*P*	R^2	β (SEE)	*P*
Model a	0.303			0.171			0.246		
White[2]		0.59 (0.17)	0.001		130.2 (66.1)	0.05		−1.64 (0.50)	0.002
Hispanic[2]		0.38 (0.17)	0.04		6.66 (68.6)	0.92		−1.28 (0.52)	0.02
BMI *z* score		−0.51 (0.22)	0.03		50.80 (88.6)	0.57		−0.38 (0.67)	0.57
Body fat (%)		0.02 (0.01)	0.15		3.82 (5.07)	0.45		−0.02 (0.04)	0.62
WBISI		−0.24 (0.09)	0.01		−62.98 (34.2)	0.07		0.89 (0.26)	0.001
Model b	0.311			0.296			0.328		
White[2]		0.40 (0.19)	0.05		−23.80 (74.0)	0.75		−0.64 (0.57)	0.27
Hispanic[2]		0.23 (0.19)	0.23		−107.3 (70.6)	0.13		−0.55 (0.55)	0.33
BMI *z* score		−0.59 (0.23)	0.01		−14.6 (84.0)	0.86		0.04 (0.65)	0.96
Body fat (%)		0.01 (0.01)	0.36		−1.31 (4.90)	0.79		0.01 (0.04)	0.72
WBISI		−0.15 (0.09)	0.13		5.44 (36.70)	0.88		0.45 (0.28)	0.12
Visceral fat (cm^2)		0.01 (0.004)	0.08		5.28 (1.42)	< 0.0001		−0.03 (0.01)	0.003
Model c	0.393			0.191			0.218		
White[2]		0.40 (0.18)	0.03		81.37 (76.06)	0.28		−1.23 (0.57)	0.04
Hispanic[2]		0.23 (0.18)	0.20		−30.47 (74.13)	0.68		−0.97 (0.56)	0.09
BMI *z* score		−0.63 (0.22)	0.005		38.29 (90.68)	0.67		−0.49 (0.68)	0.48
Body fat (%)		0.01 (0.01)	0.25		2.60 (5.17)	0.62		0.01 (0.04)	0.86
WBISI		−0.24 (0.01)	0.01		−51.15 (39.44)	0.19		0.65 (0.29)	0.03
HFF (%)		0.02 (0.01)	0.01		4.01 (2.83)	0.16		−0.02 (0.02)	0.24
Model d	0.402			0.296			0.291		
White[2]		0.32 (0.19)	0.11		−27.35 (78.35)	0.73		−0.53 (0.60)	0.38
Hispanic[2]		0.17 (0.18)	0.37		−110.3 (73.52)	0.14		−0.46 (0.57)	0.42
BMI *z* score		−0.67 (0.22)	0.003		−20.08 (86.87)	0.82		−0.11 (0.67)	0.86
Body fat (%)		0.01 (0.01)	0.37		−1.31 (4.99)	0.79		0.02 (0.04)	0.64
WBISI		−0.19 (0.10)	0.06		2.04 (40.25)	0.96		0.32 (0.31)	0.31
Visceral fat (cm^2)		0.004 (0.004)	0.29		5.13 (1.52)	0.001		−0.03 (0.01)	0.007
HFF (%)		0.02 (0.01)	0.03		0.85 (2.82)	0.76		−0.01 (0.02)	0.81

[1] WBISI, whole-body insulin-sensitivity index; HFF, hepatic fat fraction. Stepwise multiple linear regression analyses were adjusted for age and sex.
[2] Reference group was African American.

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TABLE 4
Effect of hepatic fat content, visceral fat, and ethnicity on VLDL, LDL, and HDL particle size[1]

	Dependent variable								
	VLDL size			LDL size			HDL size		
Independent variable	R^2	β (SEE)	*P*	R^2	β (SEE)	*P*	R^2	β (SEE)	*P*
Model a	0.213			0.183			0.267		
White[2]		6.04 (2.67)	0.03		−3.83 (0.17)	0.03		−0.32 (0.08)	<0.0001
Hispanic[2]		3.40 (2.77)	0.22		−0.06 (0.18)	0.75		−0.20 (0.08)	0.02
BMI z score		−4.28 (3.58)	0.24		−0.34 (0.23)	0.15		−0.10 (0.10)	0.35
Body fat (%)		−0.01 (0.20)	0.96		0.01 (0.01)	0.70		−0.003 (0.01)	0.63
WBISI		−4.52 (1.38)	0.002		0.20 (0.09)	0.03		0.12 (0.04)	0.01
Model b	0.241			0.229			0.356		
White[2]		3.01 (3.19)	0.35		−0.13 (0.20)	0.52		−0.15 (0.09)	0.11
Hispanic[2]		1.16 (3.04)	0.70		0.13 (0.19)	0.52		−0.07 (0.09)	0.39
BMI z score		−5.57 (3.62)	0.13		−0.24 (0.23)	0.32		−0.03 (0.10)	0.78
Body fat (%)		−0.11 (0.21)	0.60		0.01 (0.01)	0.32		0.003 (0.01)	0.68
WBISI		−3.17 (1.58)	0.05		0.08 (0.10)	0.39		0.04 (0.05)	0.38
Visceral fat (cm^2)		0.10 (0.06)	0.09		−0.01 (0.004)	0.03		−0.006 (0.002)	0.002
Model c	0.255			0.209			0.266		
White[2]		2.91 (3.01)	0.34		−0.26 (0.20)	0.19		−0.32 (0.09)	0.001
Hispanic[2]		1.02 (2.93)	0.73		0.03 (0.19)	0.87		−0.20 (0.09)	0.03
BMI z score		−5.10 (3.59)	0.16		−0.28 (0.24)	0.24		−0.09 (0.11)	0.43
Body fat (%)		−0.08 (0.20)	0.67		0.01 (0.01)	0.56		−0.003 (0.01)	0.61
WBISI		−3.77 (1.56)	0.02		0.18 (0.10)	0.07		0.13 (0.05)	0.01
HFF (%)		0.26 (0.11)	0.02		−0.01 (0.01)	0.15		<0.0001 (0.004)	0.97
Model d	0.265			0.241			0.366		
White[2]		1.53 (3.30)	0.64		−0.10 (0.22)	0.63		−0.18 (0.09)	0.06
Hispanic[2]		0.010 (3.10)	0.99		0.15 (0.20)	0.46		−0.10 (0.09)	0.26
BMI z score		−5.85 (3.66)	0.114		−0.19 (0.24)	0.41		−0.015 (0.10)	0.89
Body fat (%)		−0.14 (0.21)	0.52		0.01 (0.01)	0.33		0.002 (0.01)	0.79
WBISI		−3.10 (1.69)	0.07		0.11 (0.11)	0.33		0.06 (0.05)	0.24
Visceral fat (cm^2)		0.06 (0.06)	0.32		−0.01 (0.004)	0.08		−0.01 (0.002)	0.001
HFF (%)		0.22 (0.12)	0.07		−0.01 (0.01)	0.43		0.004 (0.004)	0.27

[1] WBISI, whole-body insulin sensitivity index; HFF, hepatic fat fraction. Stepwise multiple linear regression analyses were adjusted for age and sex.
[2] Reference group was African American.

distribution of HDL sizes (model b; Table 4). HFF did not explain the variability in the distribution of either the concentrations of large HDL or HDL sizes ($P > 0.05$).

DISCUSSION

In the current study, we showed that, at similar concentrations of VAT, African American youths had lower liver fat contents than did whites and Hispanics. Furthermore, liver fat accumulation, independent of VAT and insulin resistance, emerged as an important predictor in large VLDL particle concentrations seen among the 3 ethnic groups. In contrast, the contribution of liver fat to the variance in both LDL and HDL subclasses was mitigated by the greater effect of VAT.

Consistent with other reports (26, 27), our study showed ethnic differences in the distribution of large VLDL, with whites and Hispanics having much higher concentrations. However, ethnic differences in VLDL sizes were not significant. Results from our multivariate analysis revealed that liver fat content (%HFF) was independently and significantly associated with large VLDL. This is in contrast with other studies in children (6) that showed that high concentrations in large VLDL were accounted for by VAT. In those studies, the effect of liver fat, crucial ectopic fat, was not taken into account. Our study is consistent with studies (10, 28) performed in adults that indicated that liver fat is a significant correlate of triglyceride concentrations and VLDL particles, independent of VAT.

The distributions of small LDL particle concentrations and LDL sizes were comparable among ethnicities. This is in contrast to other studies that showed black children had larger LDL size particles than did white children (29). We attribute the lack of racial and ethnic differences in our study to the small sample size and perhaps because the level of obesity in the black children was rather substantial and thus may have overridden any other protective mechanisms linked to their genetic background. In all 3 ethnic groups, small LDL concentrations were twice as high as the large LDL particle concentrations, which suggested that all 3 groups may have been overproducing small LDL particles. In contrast, large HDL concentrations and sizes were significantly higher in the African American adolescents than in the other 2 ethnic groups (Table 2) in accordance with previous studies (6). The lower triglyceride concentrations in the African American group may be due, to some extent, to an increased hydrolysis of plasma triglycerides. However, in the absence of turnover studies, it is difficult to know precisely if the VLDL production and clearance are equally affected by ethnicity and obesity.

Contrary to the independent role of liver fat in predicting large VLDL, we observed the opposite for effect for small LDL and

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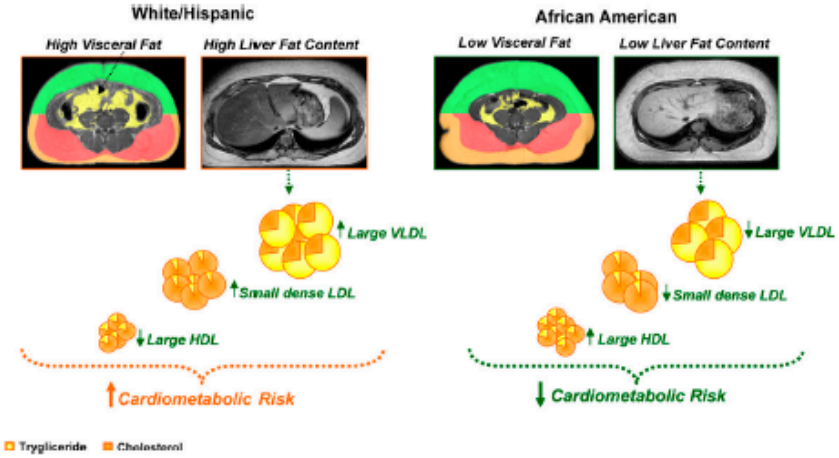


FIGURE 2. Hypothetical origin of the cardiometabolic risk profile by ethnicity in obese adolescents.

large HDL particles, namely that their concentrations were significantly more related to the amount of VAT (Table 3). Thus, depending on the type of lipoprotein, there seem to be different effects of liver fat and visceral fat in obese adolescents. Although it is conceivable that both VAT and liver fat carry independent health risks, how they may have differential effects on the various lipoproteins is unclear. The close association shown between VAT and liver fat would suggest a putative causal link, particularly in whites and Hispanics. The sustained exposure of the liver to an increased flux of free fatty acids (eg, portal theory), secondary to the enlargement of the VAT, has been often raised as an explanation of this close association between VAT and fatty liver (30). However, the validity of the portal theory has been questioned by studies that indicated that only 20% of portal vein FFA delivered to the liver is derived from the lipolysis of VAT in obese subjects (31). Therefore, another possible mechanism may be due to the greater availability of nonsystemic fatty acids derived from the lipolysis of intrahepatic triglycerides, as suggested by Fabbrini et al (14). A schematic representation of our hypothetical model explaining the origin of the cardiometabolic risk profile by ethnicity is shown in **Figure 2**.

Although the focus of the current study was mainly on how different patterns of fat distribution might be associated with ethnic differences in lipoprotein profiles, genetically driven interethnic differences in lipoprotein profiles need to be considered. Indeed, polymorphisms in human *LIPC* and *LPL* together may account for the interethnic differences in triglyceride and HDL concentrations (7, 8, 32, 33). Several studies (8, 33) have shown that the T allele at position −514 of the promoter region of *LIPC*, which is associated with lower hepatic lipase activity and higher HDL concentrations, is higher in African Americans than in whites. Likewise, common variants in the *LPL* have been shown to contribute to the ethnic differences in fasting serum triglyceride concentrations (7, 32, 34). For instance, the *LPL* −93T/G promoter common variant, which was previously reported to have a triglyceride-lowering effect, is more prevalent in African Americans than in whites (32). These findings support the hypothesis that some of the population variation in lipid traits is indeed genetic and can be attributed to variants that have different frequencies in different ethnicities (7).

Insulin resistance is known to be associated with an increased large VLDL and small LDL concentrations and a lower HDL concentration, irrespective of race and sex (5, 6). In our study, insulin sensitivity was not significantly different among the 3 ethnic groups, despite the profound differences in body fat distribution. Although insulin sensitivity was a significant determinant of large VLDL, small LDL, and large HDL, it lost significance when either liver fat or VAT were entered in the model (Table 3, models b–d).

Limitations of the current study are due to its cross-sectional design, which did not prove causality. Given the sample size, we were unable to stratify our analysis by sex, and therefore, we may have underestimated any potential sex differences in lipoprotein particles across the ethnic groups. However, all analyses were adjusted for age and sex. The study had sufficient power to conclude that hepatic fat accumulation is an important independent predictor of large VLDL concentrations. Lastly, although the lack of a control nonobese group might have enhanced our understanding of the ethnic differences in lipoprotein profiles, we believe that it would not have played an important role in the assessment of the association between patterns of fat distribution and lipoprotein profiles among the 3 ethnic groups. This is because ectopic fat in lean children is virtually nonexistent and, thus, unmeasurable.

In conclusion, VAT is closely linked to liver fat in white, Hispanic, and African American obese adolescents. Liver fat accretion, independent of visceral fat and insulin resistance, is a strong independent marker of large VLDL particles. In contrast, the contribution of liver fat to the variance in LDL and HDL subclasses was mitigated by the greater effect of visceral adiposity. The more favorable metabolic risk profile of African American youths could be linked to the lower accretion of fat in the liver and visceral compartment.

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The authors' responsibilities were as follows—ED: performed data analyses and wrote the manuscript; VN: helped with statistical analyses and the interpretation of results; RW and NS: helped with the interpretation of results and provided critical commentary on the manuscript; BP, MS, and GO: contributed to data collection; and SC: designed the study, wrote the manuscript, helped with the interpretation of results, and provided critical commentary on the manuscript. None of the authors declared a conflict of interest.

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Original Article

Timely Diagnosis of Malalignment of the Distal Extremities Is Crucial in Morbidly Obese Juveniles

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Key Words

Obesity · Children · Malalignment · Lower extremities · Temporary epiphyseodesis

Abstract

Background/Aims: To determine i) whether obesity in childhood can be related to malalignment of the distal extremities, ii) the proportion of genu valgum malalignment and abduction setting, and iii) the respective deviation dominance in children who are morbidly obese. ***Methods:*** 31 morbidly obese Caucasian children (16 males) recruited for the STYJOBS Study (ClinicalTrials.gov Identifier NCT00482924) with a mean age of 13.9 ± 0.5 years, a mean height of 162.3 ± 2.7 cm, a mean weight of 90.62 ± 5.0 kg, and a mean BMI of 33.8 ± 1.2 kg/m^2 were clinically examined using the Mikulicz line in order to assess load distribution on the knee joint. 21 participants received a whole-leg X-ray because of a clinically estimated malalignment. ***Results:*** 8/31 participants examined were diagnosed with genu valgum, 1/31 with genu varum, and 22/31 did not have any malalignment of the femur or tibia. The majority of genu valgum presentation was due to femoral deviation. Of those without malalignment, 4/22 participants had an abduction setting, while 2/22 showed an adduction of the leg. ***Conclusion:*** Genu valgum as a predominant malalignment of the distal extremities is frequent in youth with morbid obesity. Timely guided correction of angular deformity of the knee seems pivotal in order to avoid osteotomy or osteoarthritis later in life. © 2013 S. Karger GmbH, Freiburg

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Introduction

Childhood obesity is associated with a wide spectrum of medical comorbidities of significant physical and psychological impact [1]. The individual and financial costs associated with musculoskeletal conditions are substantial [2], and musculoskeletal pain has been identified as the most expensive of all disease categories in Europe [3].

Recently, obesity has been acknowledged as a key risk factor for musculoskeletal problems in children and adolescents. Obese children have an increased fracture risk [4], suffer more frequently from back, hip, and knee pain [4–6], and present with more impaired flexibility [7], changes in foot structure [8, 9], osteoarthritis [10–12], slipped capital femoral epiphysis [13], and Blount's disease [14] compared to normal-weight individuals. Lower extremity malalignment, which might predispose to osteoarthritis [10], has also been suggested to be highly prevalent in obese children [4, 5, 7, 15].

However, no studies have yet assessed these patients regarding the clinical distinction of actual malalignment from the mere abduction setting of the leg, which can be challenging in daily routine, particularly in morbidly obese patients. In addition, there is a lack of data on the prevalence and the extent of femoral and tibial deviation in malaligned extremities. This is relevant because a timely diagnosis may have immediate therapeutic implications in juveniles.

Therefore, the current study aims to determine i) whether obesity in childhood is related to malalignment of the distal extremities, ii) the proportion of genu valgum malalignment and abduction setting of the leg, and iii) the respective deviation dominance (i.e. femoral vs. tibial) in morbidly obese children.

Subjects and Methods

The study population consisted of morbidly obese Caucasian children recruited for the STYrian Juvenile Obesity Study (STYJOBS; ClinicalTrials.gov Identifier NCT00482924) at the Department of Pediatrics, Paracelsus Medical School Salzburg, Austria, from March 2007 to May 2011. None of the patients were referred for orthopedic reasons. All patients were morbidly obese, defined as a BMI > 99.5 percentile for age and sex [16], and aged between 6 and 19 years. The subjects enrolled were apparently healthy based on a complete physical examination. Exclusion criteria were chronic rheumatic disease, major trauma, or fracture of the distal extremities leading to their malalignment. 31 subjects (16 males) were eligible for evaluation (table 1). Oral consent from all participants as well as parental consent for minors was obtained.

Anthropometric Measurements

Height, weight, and waist circumferences were obtained from all children. The participants wore light clothing (e.g. shorts and a light top) and no shoes during the measurements. Standing height was measured to the nearest 0.1 cm using a portable calibrated stadiometer (SECA). Body mass was measured to the nearest 0.01 kg using calibrated electronic scales (SECA 701). The BMI was calculated as the weight in kilograms divided by the square of height in meters (kg/m^2). The degree of overweight was quantified by using Cole's least mean square method, which normalizes the BMI-skewed distribution and expresses BMI as a standard deviation (SD) score (BMI-SDS). Waist circumference was measured in a standing position with a flexible tape midway between the lower costal margin and the superior border of the iliac crest.

Clinical Orthopedic Examination

As described by Westhoff et al. [17], the distal extremities were assessed in the frontal plane by observing the standing participant from the front and from the back. The assessment of lower limb alignment, however, can be challenging in patients with excessive subcutaneous fat accumulation. Thus, the Mikulicz line was used in order to evaluate the alignment of the lower extremities. This method was originally designed to objectively assess limb alignment using long-leg X-rays [18]. In this study, the patient was positioned in supine position with outstretched legs for the initial clinical assessment. Using a piece of rope, the top end was posi-

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Table 1. Clinical characteristics of study participants (n = 31)

	Total cohort
Age, years	13.9 ± 0.5
Body height, cm	162.3 ± 2.7
Body weight, kg	90.6 ± 5.0
BMI, kg/m^2	33.8 ± 1.2
BMI-SDS	2.78 ± 0.09
Waist circumference, cm	105.9 ± 3.9

BMI-SDS = Body mass index standard deviation score.

tioned two square fingers medial to the superior anterior iliac spine and was drawn to the talocrural articulation, thereby clinically reproducing the Mikulicz line. If the rope was passing centrally through the knee, indicating a physiological burden of the joint, an abduction setting of the knee was diagnosed. If the line passed medially to the patella or medially to the intercondylar eminentia of the tibia, the setting was interpreted as genu varum; the line passing laterally to the patella was interpreted as genu valgum. In cases of clear or suspected malalignment, an anteroposterior weight-bearing long-leg X-ray was performed to distinguish between actual misalignment of the extremity and abduction setting of the leg, and to determine the respective degree of misalignment/abduction setting, as previously described by Strecker [19]. A 1° physiologic variation of the mechanical weight-bearing axis from the center of the knee joint and a 1° error in measurement was assumed. All subjects displaying an axial deviation >2° were diagnosed as genu valgum or genu varum [20]. This value is in accordance with the SD of the tibiofemoral angle, as previously reported [21–23]. In cases of malalignment, the axial deviation was also used to determine the deviation dominance (i.e. femoral vs. tibial). For this, the anatomic lateral distal femoral angle (aLDFA) and medial proximal tibial angle (MPTA) were used to describe the axes between knee joint line and the related anatomic axes in the frontal plane defined by a line drawn through the diaphyseal shaft of the femur/tibia [19]. The physiologic norm for these angles was defined as 85–90° (MPTA) and 79–83° (aLDFA) [19]. A deviation in one of the two angles indicated the center of rotation of angulation (CORA) of the malalignment.

Results

The clinical characteristics of the study participants are given in table 1. Data are given as means and SD. All patients were morbidly obese.

Alignment of Distal Extremities

10/31 (32.3%) patients showed normal alignment of the distal extremities upon physical examination, requiring no X-ray. According to investigational standards of the Orthopedic Department of the University Hospital Salzburg, an X-ray was only taken if the Mikulicz line was not centered at the patella or if the iliac crest could not be detected due to abdominal mass (21/31 patients = 67,7%). In 12 of these individuals (12/31 = 38.7%), no malalignment could be diagnosed radiographically (with 4 patients showing an abduction setting and 2 an adduction setting). 8/31 (25.8%) patients showed genu valgum and 1/31 (3.2%) genu varum (table 2).

Mechanical Axis Deviation

In 6/8 (i.e. 75%) participants, genu valgum malalignment was due to femoral malalignment, in 1 (12.5%) individual due to tibial malalignment, whereas in 1 (12.5%) participant combined malalignment of femur and tibia was detected. Of the participants without malalignment, 4/12 (33.3%) had an abduction setting and 2/12 (16.7%) an adduction of the leg (table 2). The mechanical axis deviation from the center of the knee in patients with

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Table 2. Alignment of the distal extremities (31 participants)

	n
Anatomical malalignments	
Genu valgum	8
Femur	6
Tibia	1
Femur + tibia	1
Genu varum	1
No anatomical pathology	
Clinical diagnosis (Mikulicz line central)	10
Radiographic diagnosis	12
Abduction of knee >2° to plumb line	4
Adduction of knee >2° to plumb line	2

Table 3. Mechanical axis deviation from the center of the knee

	Mean mechanical axis deviation	aLDFA	MPTA
Genu valgum (n = 8)			
Right leg	3.3 ± 0.8° (2.5–4.7°)	78.2 ± 3.7° (73.9–85.6°)	88.2 ± 1.3° (86–89.5°)
Left leg	3.4 ± 1.4° (2.1–5.8°)	79.3 ± 4.6° (72–85.7°)	87.7 ± 1.8° (84–90°)
Genu varum (n = 1)			
Right leg	3.9°	85.6°	88.1°

aLDFA = Anatomic lateral distal femoral angle (reference 79–83° [19]); MPTA = medial proximal tibial angle (reference 85-90° [19]).

genu valgum malalignment ranged from 2.5 to 4.7°on the right side and from 2.1 to 5.8° on the left side. There was 1 participant demonstrating genu varum malalignment who showed a deviation of 3.9° of the right knee.

The aLDFA ranged from 73.9 to 85.6° on the right leg and from 72 to 85.7° on the left side. The aLDFA of the participant with genu varum malalignment was 85.6°. The MPTA on the right side ranged from 86 to 89.5° and from 84 to 90° on the left side. The MPTA of the participant with genu varum malalignment was 88.1° (table 3).

Therapeutic Consequences

Of all overweight and obese juveniles with radiographically confirmed genu valgum and genu varum, 5/9 (55.6%) were recommended to undergo surgical therapy in terms of temporary epiphyseodesis using a tension plate [24]. The other participants with malalignments were either suffering from only slight malalignment (1/9, i.e. 11.1%) or complete closure of the growth plates (3/9, i.e. 33.4%). All patients were referred to interdisciplinary obesity treatment.

Discussion

This cross-sectional study assessed 31 obese pediatric patients and found that valgus malalignment with femoral deviation is frequent in morbidly obese juveniles. Early diagnosis of lower extremity malalignment seems to be crucial in obese youth in order to allow for

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temporary epiphysiodesis as well as to prevent them from osteotomy and, most importantly, irreversible osteoarthritis in later life. Interestingly, femoral deviation was more common than tibial deviation in our morbidly obese pediatric patients. This seems crucial as it might imply direct therapeutic consequences in terms of surgical axis correction and temporary epiphyseodesis.

Children and adolescents who are overweight and especially those who are obese suffer from a multitude of orthopedic complications including musculoskeletal discomfort, spinal complications such as scoliosis or lumbar hyperlordosis, slipped capital femoral epiphysis, osteoarthritis, Blount's disease, bone fractures [5, 13, 25, 26], structural changes of plantar anatomy [8], reduction in flexibility, impaired mobility, and malalignment of the lower extremities [4, 5, 7].

Among other factors, joint alignment has been described to be vital for osteoarticular health of the knee [27]. About 50% of severely obese adults (mean BMI 39.9 ± 5.8 kg/m^2) presented with marked lesions of the cartilage of the knee in an Australian study [28]. More importantly, a recent study demonstrated that morbidly obese children and adolescents with knee pain already showed marked morphological changes of the cartilages of different grades and in different compartments of the knee [29].

In general, there are two categories of hypotheses to explain the obesity-osteoarthritis relationship: metabolic and mechanical. A possible relationship between metabolic parameters of obesity and adult osteoarthritis could not be established. Yet, different paradigms have been suggested in which obesity increases the risk of osteoarthritis directly or by influencing local factors that mediate the mechanical impact of excess body weight on the knee [11]. While axial loading, as represented by BMI, was shown not to contribute to the increasing knee angles in normal, healthy-weight children [30], the results of our study confirm our assumption of a high prevalence of malalignments of the distal extremities in morbid obesity as early as during childhood. Even though there is a paucity of literature demonstrating the relationship between body mass and the magnitude of the knee angles in juveniles, our findings are in accordance with previous studies [4, 5]. However, while Taylor et al. [4] used non-weight-bearing images, full-limb X-ray pictures of the lower extremity under weight-bearing conditions with the participants in standing position were used in the current study. These conditions are more likely to reveal the clinically relevant static effect of excess weight loaded on misaligned knees. In keeping with Taylor et al. [4], the majority of our young patients with malalignment showed genu valgum. This is in contrast to adult data where most obese patients exhibit varus rather than valgus alignment [31]. Tayler et al. [4] hypothesized that even mild malalignment might lead to skeletal discomfort and pain if children are overweight or obese. In the development of the lower extremity axis, vertical pressure leads to growth, bone formation, and alignment. This value is in accordance with genu varum, is gradually aligned, and then leads to genu valgum, which reaches its maximum at the age of 3 years and decreases to normal values at around 9 years of age. Most studies on lower limb alignment in children have used the tibiofemoral angle to describe angular deformities of the tibia or femur in the frontal plane [21–23], thus depicting the anatomical axis. However, the mechanical load is best described by the mechanical axis based on the joint reference lines of the hip, knee, and ankle [32].

Given these facts, we hypothesize that overweight might not only decrease mobility and flexibility in children but may also interfere with the natural development of the bone axis so that valgus malalignment persists in a subset of patients. Thus, early-onset obesity before puberty might be a particular risk factor for malalignment and consequent orthopedic complications. There are recent data available showing that structural and physiological changes such as alterations in passive joint restraints occur during puberty. These may not only affect the type, severity, and incidence of injuries in the maturing adolescent population but also contribute to decreased mobility and flexibility in overweight children [33].

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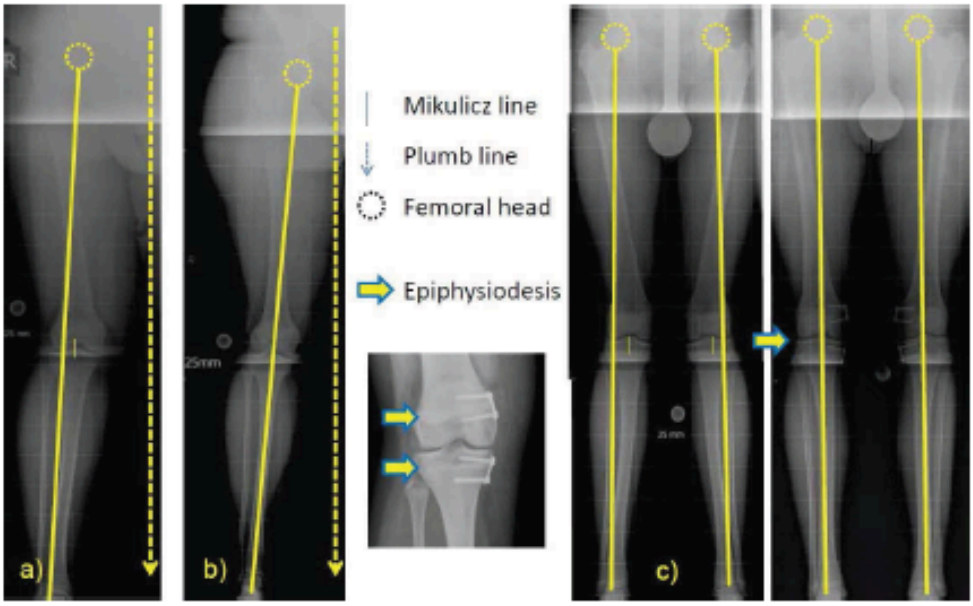


Fig. 1. Clinical presentation of alignment in morbidly obese children. **a** Genu valgum. **b** Abduction setting. **c** Epiphysiodesis to correct genu valgum (prior to and 17 months after surgery).

Due to a lack of prospective studies the long-term clinical significance of childhood knee malalignment associated with obesity has yet to be determined. However, since obesity may increase the magnitude of joint loading, joint position and alignment may influence knee-joint forces. The latter have been theorized to play a pivotal role in the progression of osteoarthritis in the obese by altering stress distribution within the joint [27]. Gushue et al. [34] and Strutzenberger et al. [35] found that obese children have greater knee moments, causing greater loading of the musculoskeletal structures compared to normal-weight children. However, Felson et al. [10] concluded that the effect of BMI might be limited to knees in which at least moderate malalignment exists. Since knee alignment has been shown to influence pain and functional deficits in adult patients with knee osteoarthritis [36], a recent long-term study assessing the relationship between BMI throughout a lifetime and knee pain in adulthood is of great interest: Macfarlane et al. [37] demonstrated that being overweight in teenage years and early adulthood is predictive of knee pain at the age of 45. In addition, a recent study could show that valgus malalignment increases the risk of knee osteoarthritis as assessed by X-ray progression as well as the incidence of lateral cartilage damage [38]. In contrast, it was reported that BMI was positively associated with the severity of joint space narrowing in individuals with varus alignment but not in those with valgus alignment when determined by full-limb radiographs in adults [11]. Westhoff et al. [17] also found that valgus alignment is less likely to cause arthritis than varus alignment.

The growth potential of the distal femur has been shown to be superior as compared to the proximal tibial physis [39]. To the best of our knowledge, we are the first to report that femoral deviation is more common than tibial deviation in obese pediatric patients. Therefore, the differentiation in tibial/femoral predominance of malalignment seems crucial as this might imply direct therapeutic consequences in terms of surgical axis correction and temporary epiphyseodesis [40, 41].

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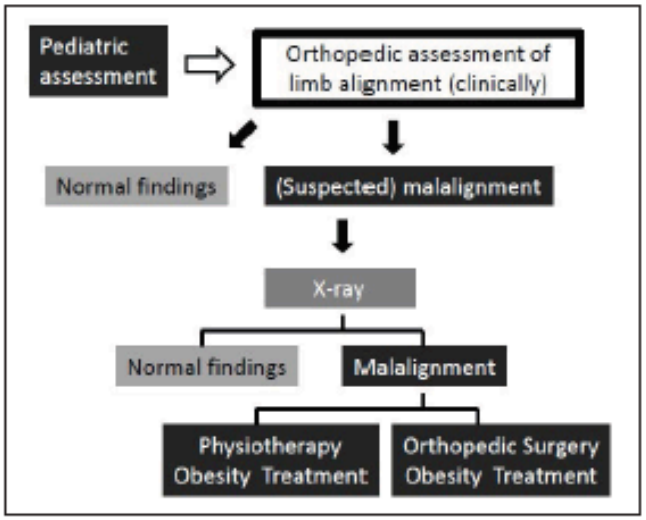


Fig. 2. Algorithm for the orthopedic assessment and treatment of morbidly obese juveniles.

Of the participants in our study without malalignment, about one third was diagnosed with an abduction or adduction setting of the legs. These children showed a physiologic mechanical axis on full-limb X-ray and a normal burden of the knee joint. Under daily clinical conditions the differentiation between mere abduction setting and actual pathologic alignment can be difficult in morbidly obese patients (fig. 1). Although the Mikulicz line is commonly used to interpret lower limb alignment in long-leg X-rays, its clinical depiction by the use of a rope offers a simple screening method in order to differentiate malalignment and abduction setting. However, this is only possible in a minority of morbidly obese juveniles due to difficulties in identifying the respective anatomic landmarks, thus making an X-ray necessary. Moreover, long-leg X-ray pictures allow for defining the degree of severity of malalignment, which is important for surgical treatment decision. However, this method has some limitations. Obesity might pose a problem in diagnosing X-ray pictures and defining anatomic landmarks because of blurred pictures of the femoral head. By holding up abdominal aprons or depicting the femoral head separately, this problem can be avoided.

In our opinion, the results of our study are of utmost clinical relevance: Almost a third of all obese juveniles assessed had a degree of valgus malalignment resulting in referral for surgical correction. In addition, some patients showed closure of the epiphyseal plate and would also have benefited from timely intervention. Diagnosis prior to closure of the epiphyseal plate allows for the comparably simple intervention of epiphyseodesis as compared to osteotomy after further maturation of the bones. While it is common consensus that timely measures to prevent early-onset cardiovascular complications of childhood obesity are necessary [42, 43], an equivalent claim seems to be necessary to allow for early diagnosis and swift treatment where knee malalignment is concerned. Current recommendations relating to the assessment of obese children lack detailed guidance for primary and secondary care as far as orthopedic comorbidities are concerned [44, 45]. Although our data can only be regarded as preliminary, the following clinical algorithm seems to deserve further studies: Juveniles who are morbidly obese should undergo a thorough orthopedic assessment including evaluation of lower limb alignment at the beginning of puberty (fig. 2). In the case of suspected or definite malalignment, referral to a pediatric orthopedic specialist for further evaluation seems mandatory to allow for timely surgical intervention if necessary. In any

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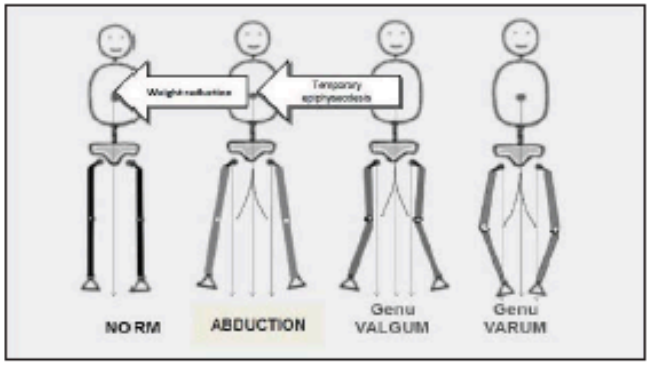


Fig. 3. Clinical presentation of lower extremity malalignment in obese children prior to closure of epiphyseal plates and treatment consequences.

case, effective obesity treatment – including bariatric surgery if indicated – must be initiated (fig. 3) [45, 46]. However, weight loss has been shown to be difficult to achieve in obese children [47]. Nonetheless, Widhalm et al. [29] proposed that pediatric patients who are obese require professional care concerning musculoskeletal disorders and most importantly physical activity programs adapted to the child's needs, skills, and handicaps. Similarly, Shultz et al. [48] stated that obese children need well-prescribed physical activity programs with less weight-bearing activities. Restoring correct lower limb alignment thus constitutes a prerequisite for knee-joint-friendly physical activity.

There are limitations to our study that need to be acknowledged. Firstly, the small study population prevents us from drawing statistically relevant conclusions regarding the prevalence of malalignment and of the specific types of deviations in general. However, the main conclusions of our study are significant but call for larger studies to obtain further information. Secondly, we cannot exclude referral bias. Most patients were sent to our clinic for metabolic assessment and not due to pain or for orthopedic evaluation.

In conclusion, morbidly obese children frequently suffer from substantial malalignment in need of correction. It is essential that children who are obese receive an accurate assessment of the musculoskeletal system in order to screen for such malalignments to identify those who might require further intervention. Obese children who are showing signs of malalignment should partake in weight management as early as possible in order to avoid progression to pathological deformity requiring surgical correction. Finally, children who are obese and have pathological malalignment should undergo early surgical intervention to achieve axial correction prior to closure of the epiphyseal plates. This might prevent children from undergoing osteotomy and experiencing further complications.

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Disclosure Statement

The authors have no potential conflicts of interest to disclose.

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Review Article

The Assessment of Eating Behaviour in Children Who Are Obese: A Psychological Approach. A Position Paper from the European Childhood Obesity Group

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Key Words
Children · Obesity · Psychological assessment · Eating behaviour

Abstract
Objective: This paper introduces health professionals to the different psychological models thought to influence eating behaviour in the absence of hunger in children who are obese and to propose a method of assessing these behaviours in practice. ***Methods:*** Clinical researchers from the European Childhood Obesity Group (ECOG) adopted an evidence-based approach to examine the literature concerning the assessment of eating behaviour in children who are obese. Studies published in English were filtered out of the medical and psychological literature from 1960 to the present, and the resulting bibliography was searched for relevant articles. Key themes from the current evidence were compiled and classified according to the underpinning psychological models. Based on the current evidence and the authors' combined clinical experience, a three-staged approach to assessment was agreed by consensus. ***Results:*** Valid and reliable tools for assessing and monitoring each of the three identified models (Dietary Restraint Theory, Emotional Eating and the Diathesis-Stress Model) are suggested for use in clinical practice, and the ECOG three-staged approach to assessing eating behaviours in the absence of hunger is described. ***Conclusions:*** This paper presents practical guidance on how to assess eating behaviour in the absence of hunger in children who are clinically obese and suggests a focus for future research.

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Introduction

Overall a child's diet should consist of both a balanced macro- and micronutrient composition as well as a balanced eating behaviour. A balanced eating behaviour encompasses eating recommended portions at fixed hours guaranteeing healthy feelings of hunger and a routine that promotes physiological growth and energy expenditure. However, a trend of snacking in the absence of hunger is observed among families in western society that may contribute to obesity via the intake of excess energy [1].

The eating behaviour of obese children who are obese can be complex. It is known that individuals who are obese may display different eating behaviours in the absence of hunger, e.g., snacking after a meal; eating 'comfort food' when feeling unhappy; eating during the night; eating too much followed by vomiting; restrained eating and meal skipping [2]. If such eating patterns occur on a regular basis or deviate too much from the regular childhood eating guidelines, we describe these behaviours as eating disturbances [3]. Although in some cases the abnormal eating behaviour can be explained by a genetic pathology or a medical disease, usually psychological models offer a better understanding.

It is important to recognize eating disturbances and their psychological antecedents in children as in many cases weight management programmes are not developed for treating symptoms of eating disturbances [4]. In the short term, some intervention studies have observed a reduction in various measures of eating pathology [5]. However, this has not been observed in the long term [6]. Furthermore, for professionals like dietitians, general practitioners (GPs) and paediatricians it is sometimes difficult to understand and treat these eating behaviours, specifically when they are related to psychological factors. Moreover, disordered eating behaviours normally occur between the ages of 6 and 15 years [7, 8]. Hence, it is prudent that timely assessment of these behaviours and their potential psychological influences be undertaken so that their progression and the subsequent need for more intensive and expensive interventions can be avoided [7].

Therefore, the present paper aims to summarize the different disturbed eating patterns observed in paediatric obesity and to review our current understanding regarding the potential psychological antecedents of these eating behaviours for non-psychologists. We must recognize that, to date, no psychological factors are identified as etiological factors in childhood obesity. Such factors identified in the literature are, however, considered to be relevant to our understanding of the psychological comorbidities associated with obesity in youth. These models can guide an appropriately thorough psychological assessment when eating in the absence of hunger is suspected. We will discuss the models, the psychological factors and the specific outcome measures to be used in an assessment. Finally, issues related to screening in a paediatric setting are discussed. The present article will mainly focus on the potential antecedents of eating behaviour in the absence of hunger as they are behaviour-specific and not necessarily related to lifestyle behaviour in general.

Observations of Eating Behaviour in the Absence of Hunger

Several psychological frameworks have been proposed to describe the origins of disturbed eating behaviour, and we selected those that evidenced their assumptions with research in children with obesity. We will discuss these below according to a questioning format which might help GPs or paediatricians to screen for eating behaviour in the absence of hunger during a clinical visit. Remarkably, different eating disturbances can occur in the same person on the same day and can even be interrelated [2].

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Binge Eating

Binge eating, defined as the ingestion of a large quantity of food accompanied by feelings of loss of control over eating, can be considered as a symptom or, when it occurs regularly, as part of a syndrome like bulimia nervosa (BN) or binge eating disorder (BED). This has recently been recognized in the DSM-5 [9]. Although binge eating can occur after feeling hungry, problematic binge eating episodes must meet three or more of the following additional criteria: eating until feeling uncomfortably full, eating large amounts of food when not physically hungry, eating much more rapidly than normal, eating alone due to embarrassment and feeling disgusted, depressed or guilty after overeating [10]. Binge eating episodes are reported in 9.3% of 'healthy' children and in up to 36.5% of children who are obese [7, 8]. According to representative European studies in youths who are morbidly obese (10–18 years), prevalence rates are approximately 10–24% for BED and 9% for BN. Although not yet fully recognized as a disorder, when binge eating occurs during the night, it is referred to as night eating syndrome (NES) [9].

Currently, at least two different models can explain binge eating depending on the observed antecedents: the dietary restraint theory (DRT) and the affect regulation theory (ART). Further psychological factors are still under study.

Restrained or Controlled Eating

Do you sometimes consciously try to limit, restrict or cut back the overall amount of food that you eat because you think this is better for your weight?

Both adults and children who are obese often report dieting attitudes and use of rigid weight loss practices and related weight fluctuations [11–13]. Whereas 'dietary restraint' refers to cognitive processes (like the cognitive preoccupation with weight, shape and food restriction), 'dieting' refers to the actual use of weight control practices to reduce caloric intake, i.e. the consumption of less than 1,200 kcal over a minimum period of 3 days. The present review includes both 'dieting' and 'dietary restraint' as separate and clearly defined variants of disturbed eating. We must acknowledge that being overweight in many people induces specific efforts to control their weight. GPs and dietitians regularly recommend dieting or 'controlling one's eating'. That entails a shift from a reliance on physiological cues of hunger and satiety to cognitive control (by the child/adolescent or by the parents) over the child's eating behaviour. In these cases, however, the cognitive control is often too strict and extremely vulnerable to disruption.

For a long time, the DRT was the leading theoretical psychological model that, based on several experimental studies, explained eating problems after following a strict diet [12]. These studies demonstrate that, after inducing emotional or cognitive loads, the cognitive control often fails resulting in an increased risk of overeating. Also, in children who are obese, dietary restraint attitudes and dieting behaviours are often observed and can be alternated with disruption and binge eating which paradoxically can lead to weight increase [7, 8, 12]. It is also hypothesized that failures of (rigid) restraint behaviour cause distress which in turn promotes more emotional eating and difficulties in discriminating real feelings of hunger and satiety. As a result, susceptibility to abnormalities in eating patterns is likely to increase, and strict dieting as well as dietary attitudes are therefore identified as 'risk variables for eating disturbances' [12]. Moreover, neurocognitive studies and cognitive research present an alternative approach based on the theory of thought suppression [14]. Thought suppression is seen as a mental control process that situates the individual into a modus of cognitive load. 'Control', with its necessity to maintain 'restrained eating' at the

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meta-level, describes how the human brain is principally unable *not* to think about something. Every 'control' thought, like 'I am *not* going to eat chocolate and chips now', activates an image of chocolate etc. in the brain, similar to a search command on a computer for 'NOT obesity' which will open all files and text passages containing the word 'obesity'. Consequently, the suppressed thoughts become even more conscious through so-called 'ironic processes' that overload the individual's mental processes and thus paradoxically the unwanted behaviour (e.g., eating more of a favourite snack having abstained from it for 24 h) [15].

To conclude, assessing dietary restraint attitudes in obesity clinics is relevant as it can guide our understanding of abnormal eating behaviour. If obesity specialists advise children to restrain their eating but fail i) to make this specific or ii) to duly recognize the history of past dietary restraint attitudes, it is possible that more rigid dieting intentions may ensue, resulting in potential psychological side-effects and loss of control [12].

Emotional Eating

Do you sometimes eat snacks when you are feeling alone or bored?

The consumption of 'comfort food' (energy-dense food due to high sugar and fat content) is often seen as a kind of avoidant stress coping. Stress arises when the demands of a situation exceed an individual's ability to cope and resolve the problem, resulting in emotional, behavioural and cognitive disturbances [16]. Besides life events, daily minor hassles are also seen as important stressors. Children who are obese often display body dissatisfaction and social isolation as stressors [17].

Feelings of stress can affect the eating behaviour [18, 19] during meals or via snacking. Specifically under mild stress, more eating is observed in 30–43% of adults and adolescents [18] leading to unhealthy food choices, high fat and sugar intake, eating in the absence of hunger and a more unbalanced eating pattern. For adolescents with a genetic risk for overweight this is seen as problematic [19]. Moreover, when the stress is accompanied by feelings of loss of control, it can lead to binge eating even in the absence of dietary restraint attitudes. Finally, stress induces increased negative mood, and this is related with poorer outcome in obesity treatment in some [20] but not all studies [5].

These observations can be explained by the ART which proposes that affective processes play an important role in eating behaviour, here defined as emotional eating [16]. ART postulates that particularly eating in the absence of hunger is to be seen as an effort to regulate aversive mood because i) food provides comfort on a psychological level, ii) reduces arousal on a biological level, iii) distracts people from their emotional state and iv) overshadows negative affects [16].

To conclude, besides assessing eating disorder symptoms and potential dietary antecedents, assessing emotional eating and – if possible – exploring its potential underlying factors (e.g., stressors, low self-esteem, negative mood, body dissatisfaction or social isolation) is relevant as it can guide our understanding of a second acknowledged pathway that leads to disturbed eating behaviour. With regard to treatment, 'emotional eaters' will need to develop self-control skills to cope with food in the absence of hunger and to manage emotional eating by identifying and understanding their underlying antecedents. In cases where the child suffers from severe stressors, it is recommended to collaborate with a psychologist.

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Craving and Addiction

Is your eating sometimes disinhibited after you have seen or smelled food?
Do you feel uncomfortable when you have not enough food at your disposal?

Besides the above-mentioned DRT and ART, according to psycho-biological theories some children who are obese may also show increased physical responsiveness to food in the absence of dieting attitudes or emotions. In these children, the smell, the taste and the presentation of food lead to an immediate reaction (i.e., eating while ignoring internal feelings of satiety) which can be characterized as reward-sensitive [21–24]. There is some evidence that individuals with obesity find palatable foods more rewarding than non-obese [25], but it remains unclear why this is so.

According to Gray's reinforcement sensitivity theory (RST) [22], reinforcement sensitivity reflects functional outcomes of the behavioural activation system which is organized primarily by the neurotransmitter dopamine. Imaging research in adults found that reinforcement sensitivity significantly predicted activation to appetizing foods (relative to bland foods) in brain areas implicated in food reward [24]. Additionally, functional magnetic resonance imaging (fMRI) data indicates that obese youths show greater activation in brain reward areas in response to visual food stimuli and in response to food consumption compared to lean counterparts [25]. These abnormal responses persist even after weight reduction. We assume that RST can explain a third mechanism underlying disturbed eating. Reward sensitivity can be measured not only via questionnaires but also by specific tasks. For example, it was proven in a Stroop task that, compared to controls, children who were obese displayed an attentional bias for food cues, which was not observed for neutral cues [26]. It was hypothesized that the observed bias reflects hypersensitivity for food cues, which can initiate or maintain dysfunctional eating.

It is important to be aware that resisting temptation for (food) rewards requires self-regulatory resources. As a result, overeating by highly reward-sensitive individuals can also be seen as a limitation of self-regulation skills through which impulses and immediate reward will rule over secondary considerations and long-term consequences [27]. Research proposes that parallels exist between obesity and ADHD in children [28, 29] as well as between obesity and other potentially addictive behaviours which are characterized by impulsive behaviour as the result of a rise in sensitivity to reward and a lack of self-regulation skills [30].

In addition, preliminary evidence described the similarities between substance dependence and disordered eating behaviour such as loss of control or overconsumption and inability to successfully cut down on consumption despite health complications and wishing to do so [31, 32]. However, the 'addiction' hypothesis is criticized as well. Abstinence symptoms, inevitably prevalent after substance abuse, have not yet been observed after overeating. Moreover, the link with addiction seems to have been ruled out recently since accurate use of fMRI shows that drugs mainly stimulate the ventral striatum and tobacco the dorsal striatum while obesity per se does not stimulate this area. Until now, the main evidence for addiction to certain food groups emanates from work with animal models where sugar consumption has been linked with behavioural indicators of dependence [33]. However, this area is a developing field, and data should be considered with caution.

We can conclude that, even in the absence of dietary restraint or emotional eating, some adolescents who are obese show an increased responsiveness to food, sometimes observed as cravings and addiction to overeating. The presence of such 'reward-driven' cravings should be considered as another, probably third pathway contributing to disordered eating behaviour. In treatment, we must be aware that resisting temptation requires enduring self-regulatory skills which can be extremely difficult to develop for children who are obese with high reward-sensitive traits even when motivated to lose weight.

Obesity Facts
The European Journal of Obesity
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Obesity is an Expression of a Family Pathology or a Comorbid Psychopathology

Has the child other problems besides obesity?

Does the family report that this child is difficult to educate?

Several authors emphasize the importance of the role of the family in the development and maintenance of obesity in children. Parents sometimes report a stressful family dynamic or indicate that the child demonstrates aggressive or coercive behaviour if rules are to be followed [34–40]. Although the dynamics between parent and child are difficult to unravel, there are three alternative mechanisms to consider.

First, parenting style in general and feeding style in particular are crucial factors in fostering a healthy lifestyle, promoting awareness of internal hunger and satiety cues and de-emphasizing extreme aesthetic thinness [37]. There is, for example, evidence that lowering the caloric load by increasing the proportion of wholemeal products or reduction of foods 'tolerated' in healthy-weight persons can have positive effects in adolescents who are obese [5]. It is possible that parents of a child with a history of obesity find it more difficult to effectively implement food rules on a daily basis compared to parents of other children and therefore may ultimately use less adequate parenting skills [34–36]. For example, Moens et al. [38] reported that, although parents of children who were overweight stated they were exerting more control on their children's feeding behaviour and an equal amount of parental support in comparison with parents of lean children, objective observations at mealtime indicated that in families of an overweight child, permissive and maladaptive control strategies were twice as likely and less parental support was displayed.

In the 1970s, Hilde Bruch [39] reported the presence of ineffective rules and discipline in families with children who are obese. Parents often use food to reinforce a child's desirable or undesirable behaviour, and this can have adverse side-effects. Also the opposite is observed in a hostile family climate where there may be subtle signs of emotional abuse. Population-based studies are needed before we can generalize these findings to all families with an obese child. We also need longitudinal studies in order to understand if i) ineffective parenting and ii) a dysfunctional family climate can trigger or sustain an obesity problem.

Second, Favaro and Santonastaso [40] found that psychiatric symptoms in mothers, unlike in fathers, were associated with the severity of obesity in their children.

Third, some children face greater challenges in receiving education than others. Such challenges include an irritable or reactive temperament in young childhood, more internalizing symptoms (e.g., more anxious feelings, more depressed mood, more psychosomatic complaints) or more externalizing symptoms (e.g., more impulsive behaviour, more aggression, more oppositional behaviour) [41]. Since the beginning of obesity research, not only psychological problems but also mental health disorders have been observed in children who are obese, and it remains uncertain how psychiatric comorbidities are related to obesity [41–43]. One way of testing the link is by evaluating what happens if the child's obesity problem is treated. In a study by Van Vlierberghe et al. [43], it was shown that a substantial number of adolescents still suffered from mental health problems after completing obesity treatment. Meta-analyses indicate a bi-directional process whereby mental health disorders can be either a contributing cause of obesity or a side-effect thereof [44]. Although several theories based on longitudinal research exist to understand the development of mental health problems in a child and their family, we propose the diathesis-stress model (DSM) for understanding mental health problems in children with obesity. In line with others [45], we propose that being overweight in early life in a western society which promotes the thin ideal might lead to negative feedback and low self-esteem and that this can form a 'scar' (a diathesis), making these children more vulnerable when confronted with new stressors (like bullying or family conflicts). Later in life, during the transition to adolescence new school demands, peer

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relations, 'leaving home' and autonomy are expected, thus challenging the child's survival skills and possibly leading to the development of psychopathology in vulnerable individuals confronted with stress. In line with this so-called diathesis-stress perspective on psychopathology, the 'spirit of the times hypothesis' [45] (characterized by a thin ideal and strong expectations regarding school and social performances for all children) predicts a general increase in psychological problems in overweight individuals as both a breeding ground for diatheses and higher stress levels are created.

To conclude, irrespective of the relationship between mental health problems and overweight and with respect to the incidence of stigmatization towards overweight people in western society, screening for family problems and both internalizing and externalizing symptoms appears to be appropriate. In practice, when parents complain they have a 'difficult child', it will be necessary to help the parents understand their child and strengthen their parenting skills.

Recommendations for a Psychological Screening in a Paediatric Obesity Clinic

Although National Institute for Health and Care Excellence (NICE) guidelines [46, 47] on the clinical assessment of childhood obesity and eating disorders are informative, they lack specific detail. As such, the present recommendations could be seen as an extension of the guidelines (see [46] pp 38–41 and [47] p 9).

Translated to the paediatric obesity practice, our proposed approach involves three stages: after indications of eating problems during an initial interview (stage 1) a screening session is organized with the agreement of the parents and with rating scales or questionnaires to select potential cases for further assessment by means of a cut-point score (stage 2). Third, a referral for further assessment is indicated for those participants exceeding the cut-points whereby a second administration of the questionnaires and a structured interview by a trained psychologist is recommended (stage 3). As families may often not be aware of the importance of eating behaviour and underlying psychological health for their child's overall health, it will be important for the clinician to highlight how obesity can affect multiple domains of health. Because there may be an initial lack of acceptance of questioning or assessment of these issues, the clinician must always approach the issue with sensitivity. It is imperative that the clinician addresses the child and family in an appropriate, child-friendly manner using understandable language and concepts. Fostering an environment of support and understanding is essential in order to gain accurate insight into child and family life and for establishing trust early on.

Stage 1 of Assessment

In order to conduct an evidence-based holistic assessment of children and adolescents who are clinically obese, we propose that a number of general questions be used in stage 1 to capture whether or not eating behaviour is disturbed. Such screening questions can address the aforementioned psychological models (M) which appear to underpin disordered eating in children who are obese. If one of the following five questions elicits a positive response, stage 2 of the psychological screening may be indicated:

M1. Does the child report eating large amounts of food or loss of control over his/her eating?

M2. Is the child preoccupied with restricting food, dietary restraint attitudes or severe weight and shape concerns?

M3. Does the child reveal emotional eating patterns? Has this been observed by the parent?

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M4. Does the child show a higher degree of disinhibition, display a specific responsiveness to food cues or report to be addicted to overeating?

M5. Are there family problems related with the parenting situation of the child, or does the child show internalizing or externalizing problems?

Stage 2 of Assessment

To identify at-risk children, mental health professionals need reliable and valid screening methods for further identifying behavioural and emotional problems in children. In-depth observations or interviews are generally neither very reliable nor cost-effective [48, 49]. Therefore, rating scales are seen as 'gold standards' for monitoring youth with potential mental health problems via parental report (all ages) or child report (all children ≥8 years) and to highlight potential cases for further psychological assessment. To make it easy for clinicians to judge children's functioning, each scale score of a screening instrument is only relevant when it refers to percentiles or T-scores that enable to compare a specific child's raw score with normative samples. Also cut points are important markers for identifying an at-risk child. For example, Achenbach et al. [49] who developed one of the most widely used screening instruments for psychological problems in children suggest that a T-score on the broad-band scales greater than 63 is the cut point and generally indicative of problematic behaviour.

Although rating scales are designed to provide information about the presence and severity of psychological symptoms, they cannot by themselves yield a diagnosis. Specificity and sensitivity still vary across instruments, with an estimated sensitivity of 0.66 and an estimated specificity of 0.83, indicating that numbers of false-positive and false-negative results are still quite large [48, 49]. Therefore, the use of a 'multiple-stage' strategy in the assessment of psychopathology has been recommended.

We suggest to use age-appropriate screening measures which verify the answers elicited by the five interview questions in stage 1. A variety of psychological questionnaires (10 min each), tasks (20 min each) and interviews (45 min each) can be used. Some measures are completed by the child and some by the parents, and for some both a child and parent version is available. Multi-informant testing with both the child's and the parent's perception on the same domains is always better compared with one perspective. For each hypothesis there is a number of outcome measures with established psychometric properties (see further details on the website of the European Childhood Obesity Group (ECOG)). However, we cannot burden a paediatric consult with too many tests and interviews for a child. In stage 2 of assessment, we recommend that the clinician screens for the different psychological models using only one instrument for the child and one for the parent. For this task, for example the Dutch Eating Behaviour Questionnaire (DEBQ) (child version) combined with the Child Behavior Checklist (CBCL) (parent version) is most efficient as it can help to test 4–5 models at once [49, 50]. Based on the resulting scores of the DEBQ and CBCL, moving to stage 3 of assessment may be indicated.

Stage 3 of Assessment

Where disordered eating is identified during stage 1 and stage 2 of clinical assessment, if there appear to be difficulties within the child or the home environment that could interfere with the treatment and when the assessing clinician does not feel adequately skilled, it is appropriate to discuss with the parents the option of referring the child and family to a suitably qualified paediatric psychologist for more in-depth assessment and treatment (stage 3). Completing stage 3 of assessment will vary in centres depending on access to psychology experts. A qualified paediatric psychologist means that this expert received scientific training in evidence-based assessment and treatment (preferably with a cognitive-behavioural

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approach) or in some of the well-evaluated family therapy models. Initial assessment may also identify cases where the parents require additional assessment and support for themselves (e.g. to address coping skills, parenting skills, substance dependence, depression etc.) making referral to adult specialists advisable. In stage 3, we recommend screening the psychological models via the following outcome measures:

For M1–M3: Besides the DEBQ child, a second instrument is the DEBQ parent version. If possible, double-check with a standardized interview.

For M4: Besides the DEBQ child, a second instrument is the DEBQ parent version. If possible, double-check with Behavioural Inhibition System (BIS) / Behavioural Activation System (BAS) scales [23].

For M5: For assessing family problems, use parental rejection measures. If possible, double-check the child's perspective via interview or observation. For assessing mental health problems in a child, the CBCL is a good instrument. If means are available, double-check with an interview.

Upon completion of the 3 proposed stages of assessment, the team will have a better understanding regarding the optimal treatment the child/family needs. Based on the assessment outcome, onward referral may be warranted.

Red Flags for Onward Referral

If initial screening identifies any issues where child protection might be of concern (emotional abuse, physical abuse, bullying, self-harm or life-threatening issues), it is recommended that prompt referral to appropriate services is undertaken. Also, if the child gains or loses considerable weight in a period of 6 months or has problems in the physical processes of eating such as difficulty with chewing or swallowing, referral may be indicated. Finally, some specific items included in the screening instruments can be helpful for identifying red flags that will require referral to a more specialized child/adolescent psychiatric team (e.g. vomiting, stealing food, nightmares, suicidal thoughts).

Discussion

In this review article, we summarized the different disturbed eating patterns observed in paediatric obesity and reviewed our current understanding regarding the psychological antecedents of these eating behaviours. Although multifactorial biological, societal and environmental factors influence the development and progression of obesity, there is evidence in the scientific literature regarding the plausible psychological antecedents to the development of disordered eating in children who are obese. Such factors should be considered when attempting to manage obesity in an individual child in a clinical setting. We further recommend that treatment programmes pay attention to these psychological factors as eating disturbances and their emotional precedents predict binge eating onset in adolescent girls [19] and are associated with the development of full-syndrome eating disorders. Also, eating disturbances can be linked to worse obesity treatment outcome [4–6], and binge eating itself has been associated with excessive weight gain [7]. Similarly, increased negative affect can relate to poorer obesity treatment outcome in some [20] but not all studies. When a child indicates eating behaviour in the absence of hunger, we suggest to test different possible psychological models via a three-stage approach. Such evaluation may be important in order to provide the child with optimal obesity treatment. Currently, childhood obesity interventions focus on improving impulse control by means of learning self-regulation skills such as self-obser-

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vation, self-instruction, self-evaluation and self-reward in addition to standard care (dietary as well as physical activity advice) and cognitive behavioural lifestyle intervention programmes [51]. Nevertheless, for some children who are obese, these vital skills seem to be hard to implement and maintain, particularly if they suffer from associated psychological problems. Consequently, we suggest integrating a number of psychological models into the holistic assessment:

Firstly, DRT proposes that we must help our patients to cease unhealthy dieting and pay specific attention to unhealthy eating attitudes or challenge them extensively via cognitive techniques. Secondly, the ART teaches specific emotion-focused techniques for adequate affect regulation and stress management like planning difficult situations and choosing problem solving or relaxation as alternatives to emotional eating. Finally, according to Gray's RST it is important to train impulse-control resources as such impulses are an important source of failure in self-regulation skills. Recently it was shown that novel treatments, including computer-based training, open hopeful horizons [52]. Several review papers also focused on family-based approaches in the treatment of childhood obesity. All studies (see the most recent Cochrane review [51]) point at significant and clinically meaningful weight outcomes of family-based lifestyle interventions compared to standard care in both the short and the long term. In addition, there is no question that, apart from the amount and type of food children eat, the physical fitness gained through physical activity and play is an important predictor of health, obesity and physical comorbidity. Similar to the appropriate onward referral to a psychologist for disordered eating behaviour, referral of the child to a paediatric physiotherapist for an age-appropriate physical fitness assessment will likely be indicated. Additionally, some children who are obese can be 'psychologically healthy', with no eating disorders or addiction, and have a good quality of life with preference for healthy nutrition and high intrinsic motivation for physical activity. Consequently, these children do not need extra psychological help. From other areas of prevention, we know that, in principle, salutogenic thinking is more successful than pathogenic controlling. Therefore, in future research we need to study also how we can differentiate subtypes of children according to the absence or presence of certain symptoms.

No psychological variables are identified as etiological factors in childhood obesity. However, the psychological frameworks identified may be important for understanding the associated psychological comorbidities that can interfere with obesity treatment even in motivated children. Given the importance of optimizing evidence-based obesity interventions, we propose that all children being assessed for clinical obesity are screened for eating disturbances. Further, we recommend that research examining the psychological factors related to the development of eating in the absence of hunger be undertaken. In general, psychological screening must avoid causing harm, and our suggested screening questions as well as our three-stage approach can assist clinicians in their systematic screening of disturbed eating behaviour. This method of screening should be tested, however, and future research on the effects of such an approach on the child, on the family and on treatment outcome is warranted.

Disclosure Statement

The authors report no conflicts of interest.

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APPENDIX VI.
SMARTPHONE STUDY MATERIALS

Screenshot of website developed for the Smartphone study



Smartphone study information leaflet



What will I have to do?

The W82GO! Programme lasts for 12 months and so does the study. You have already had your assessment done so that's stage 1 complete!

By partaking in the study you will get a smartphone and if you are in the smartphone group you will have your phone service paid while you are in the study. In the smartphone group you will need to use our app everyday to set goals and make challenges for yourself!

If you get picked for the Smartphone group you will need to come into the hospital 7 more times and if you are in the W82Go group you will come in 11 more times during the year.

Privacy

The information that we collect from this study will be private. It will not be shared with anyone except the research team, and your medical team.

Summary

- Voluntary study to test smartphone application
- For patients who have been diagnosed with clinical obesity
- For children over 12 years
- Treatment delivered with W82GO group programme OR by phone application
- Treatment will last a year

More information

Please ask the research team questions at any time or contact us at the details below.

Contact Details

Grace O'Malley,
Physiotherapy Dept, Temple Street,
Phone: 01 8784563;
Email: Grace.O'Malley@cuh.ie
www.w82go.ie

Smartphone Study Information

Temple Street | 140

Help me get healthy!

Can a smartphone application help teenagers to become healthier?





Obesity

Adolescent obesity in Ireland has now become a major problem. Children who have too much fat in their bodies have more risk of joint pain, early signs of heart disease & low self-esteem, and as adults may have higher risks of cancer, and type-2 diabetes. In Temple Street we have been treating obesity successfully. We now need to see if there is a better way of delivering our treatment.

Smartphone Study

We are running a study to test whether treatment for obesity delivered in person (W82GO! Programme) is better than treatment delivered directly to patients using a smartphone. We will do this be asking patients and their parents to take part in our smartphone research study.

Smartphone Study

A research study is something like a science project. When we want to learn more about a disease or treatment, we need to study people's bodies to find out how the treatment works.

In order to decide whether you want to be a part of this research study, you should know enough about it. This leaflet gives you detailed information about the research study, which a member of the research team will discuss with you. Children and teenagers over 12 years will be invited to take part. If the child and parent want to take part, they will be asked to sign a consent form. If you decide not to take part, it's okay and you can have our usual treatment. Even if you say "yes" to the study now, you can change your mind later and it's still okay.

If you decide to take part you and your family will either do the W82GO programme or use the smartphone application at home yourself. Even if you get the smartphone application, you will need to come into the hospital so that your height and weight can be measured.

We will have to divide children up equally (like tossing a coin) to make sure the groups are divided up by chance.

Smartphone study parental consent form

Principal Investigator: Grace O'Malley MSc MISCP
NAME:
DOB:
HOSPITAL UNIT NUMBER:

PERMISSION FOR PARTICIPATION IN A RESEARCH PROJECT
THE CHILDRENS UNIVERSITY HOSPITAL DUBLIN

Title: An Investigation of the effectiveness of weight management delivered using a portable device

Principal Investigator:	Grace O'Malley M.S.c, M.I.S.C.P
Organization:	The Children's University Hospital, Temple Street
Funding Source:	The Health Research Board of Ireland and The Children's Fund for Health, CUH

This Informed Consent Form has two parts:

- **Information Sheet (to share information about the study with you)**
- **Certificate of Consent (for signatures if you agree that your child may participate)**

You will be given a copy of the full Informed Consent Form

PART I: Information Sheet
Introduction

I, Grace O'Malley work in CUH as part of a team that delivers weight management to children and adolescents. We are doing research on childhood obesity and how best to treat children who are referred to the hospital. I am going to give you information and invite you to have your child participate in this research. You do not have to decide today whether or not you agree that your child may participate in the research. Before you decide, you can talk to anyone you feel comfortable with. There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me the study doctor or the staff. Once you understand the study, you will be asked if you want your child to participate; if so, you will be asked to sign this form.

Purpose of the Study

Childhood obesity in Ireland has now become a major problem with 17.8% of children aged 4-13 years described as overweight and 6.8% as obese. Short-term consequences of obesity include asthma, type 2 Diabetes, joint pain, high blood pressure, early signs of cardiovascular disease, low self esteem, and depression. Long-term consequences include a greater likelihood of being an obese adult and a greater risk of cancer and cardiovascular disease. The purpose of this research is to determine whether treatment delivered in person is more effective than treatment delivered in person plus with a smartphone application. We want to test whether our application works as this might be useful for other adolescents around the country who need treatment.

Type of Research Intervention: A study to compare face-to-face treatment with a smartphone application for treatment

Principal Investigator: Grace O'Malley MSc MISCP

Participant selection

Multidisciplinary treatment for childhood obesity has been proven to be successful, though no such treatment has been tested in Ireland. As the number of children who are obese continues to rise, we need to develop a variety of treatment strategies so that more children can access treatment that is proven to work. Because of how children grow and develop, we can't assume that delivering our treatment programme using a smartphone application will work. Because your child may develop complications due to having excess fat tissue in his/her body, we are asking if you would allow your child to participate in this study. By joining the study we will be able to test whether our application works and helps the health of children.

- ***Question:*** *Do you know why your child has been identified as a potential research participant? Do you know what the study is about?*

Voluntary Participation

Your decision to have your child participate in this study is entirely voluntary. It is your choice whether to have your child participate or not. If you choose not to consent, all the services you and your child receive at this hospital will continue.. You may also choose to change your mind later and stop participating, even if you agreed earlier, and the services you and/or your child receives at the hospital will continue.

- ***Question:*** *If you decide that you do not want your child to take part in this research study, do you know what your options for him/her are? Do you know that you do not have to accept that your child takes part in this research study? Do you have any questions?*

Description of Procedures

A. Description of the Treatment Our current multidisciplinary outpatient group treatment programme (W82GO) has been shown to be effective in improving the health of children who are obese. The effectiveness of our recently developed smartphone application has not yet been tested fully. We want to compare the two forms of treatment in a group of teenagers, and this is why we are doing this research. The hospital programme involves team members from the departments of dietetics, physiotherapy, general paediatrics, nursing and psychology, thus it is called a multidisciplinary team programme. Those attending the group programme will come to the hospital for 2-hours once per week for 6-weeks (Phase 1) and then at 3-, 6- 9- and 12-months (Phase 2).
Those receiving the smartphone app will attend the hospital for the first 6 weeks of treatment (Phase 1) and then will receive the smartphone application for Phase 2 of treatment. They will come to the hospital for measurement only at 3-, 6- 9- and 12-months . The application is based on studies that have been shown to be successful for improving the health of children who are overweight/ obese but is delivered via a smartphone and does not require the child to come into the hospital as often for treatment. A member of the clinical team will work with your child on the hospital-end of the smartphone application. There are no known side effects of either of these treatments.

Because we do not know if the smartphone treatment is better than the currently available treatment, we need to make comparisons. Children taking part in this research will be put into groups, which are selected by chance (randomized), as if by tossing a coin. One group will get the usual treatment (W82GO Group Programme) and the other group will get Phase 1 of the group programme PLUS the smartphone treatment programme. This is the best way we have for testing the treatment without being influenced by what we

think or hope might happen. We will then compare which of the two has the best results. The study team will be looking after you and the other participants very carefully during the study.

B. Description of the Process You and your child will need to visit the hospital between 5 and 15 times over 12-months during the study. Every effort will be made by the study team to ensure that you and your family are facilitated regarding appointment times. You may stay with your child during each of the visits and during the procedures.
Your child has previously had a blood test to screen for any abnormalities or to indicate risk of diabetes or heart disease. This test will need to be performed again in 12 months. It will be performed early in the morning when your child is fasting (has not eaten since 10pm the night before. An experienced phlebotomist will complete the test and numbing cream will be used to minimize any discomfort. The samples obtained during the study will be only used for this study. Any abnormalities that are found will be detailed in your child's medical chart and discussed with the referring doctor, you and your GP.

The other measurements that we will take are part of the child's usual clinical care. They will be performed two times during the study: at the beginning, and at 12-month follow up.

Assessment of Body Composition
Your child's height and weight will be measured along with a measure of waist circumference. From these measures, your child's body mass index will be calculated. We may also ask your child to step onto a Tanita scale, which is a special scale that delivers a very mild electrical current that your child won't be able to feel. This will allow us to measure the amount of fat and muscle in your child's body. Measurement takes 5 minutes.

Physical Activity Level
Your child will be asked to complete a physical activity questionnaire. You will also be asked about the amount of sleep your child gets. These forms take 10 minutes. Your child may also need to wear an activity monitor on their wrist for 7 days.

Motor Skill
Your child's balance and coordination will be assessed using a balance test, which takes 10 minutes

Nutrient Assessment
You and your child will answer questions regarding the foods your child eats, and the way food is eaten inside and outside the home. This assessment will make sure that your child is not lacking in any of the essential nutrients required for healthy growth and development. This takes 15-20 minutes.

Cardiovascular Health and fitness
Your child's blood pressure will be taken. After this your child will be fitted with a heart-rate monitor and will complete a walking test on a treadmill to measure his/her fitness. This test lasts between 10 and 20 minutes depending on how fit your child is.

Psychosocial Health
The team psychologist will meet with you and your child to complete a questionnaire to assess self-esteem and quality of life. This takes 20-30 minutes.

We will follow your child for a maximum of 1.5 years from the time of enrollment. The studies outlined above will be undertaken three times (once) If your child reaches the age of 18 before completing all tests, he or she will be asked to sign an adult consent form.

Duration

The research takes place over 12 months in total. During that time, it will be necessary for you to come to the hospital between 9 and 15 days, for up to 2 hours each day (depending on which group your child is assigned to).

- ***Question:*** *Can you tell me if you remember the number of times that we are asking you to come to the hospital to complete the treatment? The research project? How many blood tests will your child need to have? How much blood will be taken from your veins, using a syringe and needle? Do you have any other questions? Do you want me to go through the procedures again?*

Side Effects

The group treatment programme and smartphone application do not have any known side effects. However, we will follow your child closely and keep track of any unwanted effects or any problems throughout the study. We will give you a telephone number to call if you notice anything out of the ordinary, or if you have concerns or questions. You can also bring your child to this hospital to see me.

Risks and Inconveniences

Laboratory Studies By participating in this research it is possible that your child may experience some discomfort such as the discomfort of the injections. There may be a slight hardening and/or swelling where the needle stick goes into the skin. This should disappear in one day. If pain is a concern, we can use a special numbing medicine that will minimize the pain. If inflammation of the vein (also called phlebitis) does occur, application of a warm soak to the site and elevation of the arm will help. Very rarely, a child may faint, or more likely become lightheaded or nauseated, when the blood is drawn. Although also very rare, it is possible that your child may feel nauseated, get a headache, or feel shaky or lightheaded during the blood test. All blood tests are drawn while your child is sitting or lying in bed in case dizziness does occur.

Weight and Height Measurement Some children may feel uncomfortable having their weight measured. To reduce discomfort, children will be measured in private and they will have the option of knowing their weight or not.

Fitness Test This is a common test to evaluate fitness in all age groups and does not pose any additional risk to overweight or obese individuals. Although this test requires a near-maximal physical effort, and is therefore tiring, this feeling is short-lived. Your child may have sore muscles after the test. The exercise staff will go over stretching exercises with your child to minimize the chance of muscle stiffness.

Telemedicine As teenagers in the smartphone group will receive an smartphone 4 for use during the 12-month study risks associated with the use of a web-enabled device should be considered. As the smartphone treatment programme will work alongside an Internet server, participants' privacy will be maintained to the greatest extent possible, however it will be impossible to guarantee complete data security. A password-protected server will be used, possible intrusions will be monitored and data will be removed from the server after programme completion. The application is also equipped with a privacy feature that automatically logs

users out of it after 30 minutes of inactivity. If your child is in the smartphone group you will need to take responsibility for the phone and ensure that your child does not access inappropriate matieral (e.g. explicit material etc.We recommend that all parents monitor internet use by their teenager via the smartphone as they would when their child uses a home computer. Data security and confidentiality will be ensured as per Irish and EU regulations. In very rare instances, security protocols could fail, causing a breach of privacy of personal information, phone service interruption or technical difficulties.

- ***Question:*** *Do you understand that your child may have some inconveniences such as discomfort during the blood test? Do you have any questions?*

Benefits

If your child participates in this research, he/she will have the following benefits: a greater knowledge of his/her fitness level and ability to improve this improved; access to a structured exercise program which will yield benefits to his/her health; a treatment package that he/she takes with him/her everyday (if in the smartphone group); the use of an smartphone 4 for 12-months during the study period; health improvements due to the treatment; increased knowledge regarding his/her health and well-being. In addition, your child's participation will help us to determine whether treatment can be delivered remotely using a telemedicine approach(smartphone) and this may help lower the cost of treating childhood obesity and allow more children and families to access expert care. Finally, participation in the study would benefit society as a whole as the results may indicate that treatment is effective in reducing the negative effects of obesity in children which may impact generations to come.

Reimbursements

You will be provided with the following incentive to take part in this research: Each child in the Group Treatment will receive a smartphone for use on their own phone provider (Vodafone / O2 etc). Those in the smartphone group will receive a smartphone plus phone service with Vodafone for 12-months.

- *Question: Can you tell me if you have understood correctly the benefits that your child will have if you allow him/her to take part in the study? Do you understand that your child may or may not be chosen to receive the smartphone intervention? Do you know what reimbursement you or your child will receive for completing the study? Do you have any other questions?*

Confidentiality

The information that we collect from this research project will be kept confidential. Information about your child that will be collected from the research will be put away and no-one but the researchers will be able to see it. Any information about your child will have a number on it instead of his/her name. Only the researchers will know what his/her number is and we will lock that information up with a lock and key. It will not be shared with or given toanyone except members of the research team, the CUH Medical Laboratory; CUH medical record staff and your child's referring doctor. Any identifiable information that is obtained in connection with this study will remain confidential and will be disclosed only with your permission. Examples of information that we are legally required to disclose include abuse of a child or certain reportable diseases.
Data will be stored on password-protected computers, which are accessible only to members of our research team and those involved in managing thesecure on-line database. Blood samples will be labeled with your child's initials and medical record number and will be stored in laboratories that are locked when not in use. If research blood is sent to outside laboratories for analysis, the samples will be de-identified, and the code

will be stored on password-protected computers accessible only to members of the research team. We may use measurements and lab values (such as percent body fat, cholesterol, liver function tests, and tests to check your child's risk for cardiovascular disease, etc.) from your child's medical records. This will help give us a more complete picture of risks associated with obesity, diabetes, liver disease, and cardiovascular disease. Data from these studies may be shared between members of our research group. When the results of the research are published or discussed in conferences, no information will be included that would reveal your child's identity unless your specific consent for this activity is obtained.
Information obtained from this study that is relevant to your child's medical care will be placed in your child's medical record at The Children's University Hospital and, if appropriate, in your child's Obesity/Endocrine chart as well. Such information includes relevant blood tests, and results of the body composition measurement. Representatives from the CUH Human Investigation Committee and the Health Research Board may inspect study records during internal auditing procedures. However, these individuals are required to keep all information confidential.

- ***Question:*** *Did you understand the procedures that we will be using to make sure that any information that we as researchers collect about you and/or your child will remain confidential? Do you have any questions about them?*

Sharing of the results

The knowledge that we get from this study will be shared with you before it is made widely available to the public. Confidential information will not be shared. There will be small meetings in the community and these will be announced. Afterwards, we will publish the results in order that other interested people may learn from our research.

Right to Refuse or Withdraw

You do not have to agree to your child taking part in this research if you do not wish to do so and refusing to allow your child to participate will not affect your treatment or your child's treatment at The Children's University Hospital in any way. You and your child will still have all the benefits that you would otherwise have at this hospital. You may stop your child from participating in the research at any time that you wish without either you or your child losing any of your rights as a patient here.

Alternatives to participating

If you do not wish your child to take part in the research, your child will be provided with the established standard treatment available at the hospital. Children who are obese are assessed and reviewed every 3-6 months in outpatient clinics.

In Case of Injury

In the event that your child is injured from being in the study, we will treat his or her injuries. No additional financial compensation is available. You do not give up any of your legal rights by signing this form.

Who to Contact

Please take the time to read this form and make sure that you and your child understand it. Feel free to ask any questions you or your child may have. Your signature below indicates that you have read the above explanation of the procedures, that your child has given his or her voluntary assent to participate in this

Principal Investigator: Grace O'Malley MSc MISCP

PART II: Certificate of Consent

Certificate of Consent

I have been invited to have my child participate in research of obesity treatment at The Children's University Hospital.

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily for my child to participate as a participant in this study.

Print Name of Participant_____

Print Name of Parent or Guardian_____

Signature of Parent or Guardian _____**Date** _____

Day/month/year

If illiterate
A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb print as well.

I have witnessed the accurate reading of the consent form to the child and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

*Print name of witness*_____ *AND* *Thumb print of parent*

Signature of witness _____ Date _____

Day/month/year

Statement by the researcher/person taking consent
I have accurately read out the information sheet to the parent of the potential participant, and to the best of my ability made sure that the person understands the study procedure.
I confirm that the parent was given an opportunity to ask questions about the study, and all the questions asked by the parent have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this form has been provided to the participant ☐

Print Name of Researcher/person taking the consent_____

Signature of Researcher /person taking the consent_____

Smartphone study adolescent assent forms

Principal Investigator: Grace O'Malley MSc MISCP

Name:
DOB:
Hospital Unit Number:

PERMISSION FOR PARTICIPATION IN A RESEARCH PROJECT

Title: An Investigation of the effectiveness of weight management delivered using a portable device

This informed assent form is for children between the ages of 12 - 17 who attend The Children's University Hospital and who we are inviting to participate in the research study above.

Principal Investigator: Grace O'Malley M.S.c, M.I.S.C.P
Organization: The Children's University Hospital, Temple Street
Funding Source: The Health Research Board of Ireland and The Children's Fund for Health, CUH

This Informed Assent Form has two parts:
Information Sheet (gives you information about the study)
Certificate of Assent (this is where you sign if you agree to participate)
You will be given a copy of the full Informed Assent Form

What is a Research Study?

A research study is something like a science project that you might do for school, except more complicated. When doctors want to learn more about an illness or a disease, they need to study people's bodies to find out how they change as they get better or worse. The research might help doctors learn more about the illness or disease and how to treat it better.

In order to decide whether you want to be a part of this research study, you should know enough about its risks and benefits. This consent form gives you detailed information about the research study, which a member of the research team will discuss with you. Once you understand the study, you will be asked if you want to participate; if so, you will be asked to sign this form.

Why Do You Want Me to be in this Study?

We are doing this study to learn more about how treatment can help children who are overweight. We also want to find out if a new part of our treatment works when it is given using a smartphone application.

Participation is voluntary: Do I have to do this?

You don't have to be in this research if you don't want to be. It's up to you. If you decide not to take part, it's okay and nothing changes. This is still your clinic, everything stays the same as before. Even if you say "yes" now, you can change your mind later and it's still okay.

QUESTION: *Do you know that you do not have to take part in this study? Do you have any questions?*

I have checked with the child and they understand that participation is voluntary____(initial)

Principal Investigator: Grace O'Malley MSc MISCP

Purpose of the Study: Why are you doing this study?

Childhood obesity in Ireland has now become a big problem. Child who have too much fat tissue in their bodies can get asthma, pain, raised blood pressure and may not feel as happy or healthy as other children. They may also be unhealthier when they become adults. We treat children who have too much fat tissue in their bodies using a Healthy Lifestyles programme. We have also developed a smartphone application for treatment and we want to test whether the application works as well as our programme.

Procedures: What is going to happen to me?

Our Healthy Lifestyles programme (w82GO) runs over 12 months. For the first part you come with your parent(s) for an assessment. Then you come on Wednesday evenings for 2 hours, each week for 6 weeks (Part 1). Then you come to clinic again 3-months, 6-months and 9-months later (Part 2). Finally you come to be re-measured at 12-months. If you decide to take part you and your family will either do the W82GO Group programme (Part 1 and 2) or you will do Part 1 and then for Part 2 you will use the smartphone application at home yourself. Even if you get the smartphone application, you will need to come into the hospital so that your height and weight can be measured.
Because we don't know which treatment is better we need to compare children who do the full group programme with those who get the smartphone application. We will have to divide children up equally by chance (like tossing a coin) to make sure the groups are the same.

For the assessment you will do the following things:

Blood Test: You have already had a blood test as part of the doctor's assessment. You will need to have this once more in 12-months time. You will come into clinic fasting (have nothing to eat after 10pm the night before) and get a blood test. This is important as will tell us what the level of fat and sugar in your blood is. This may feel like a pinch but the nurse who takes the blood is very gentle and will use numbing cream so that it is not sore.

Body Measures Your height and weight will be taken and from this we will make some calculations. We also may ask you to stand on a special scales, which will tell us how much fat tissue is in your body. This takes 5 minutes.

Physical Activity Level We will ask you to fill out an activity questionnaire and a sleep form, which takes 10 minutes. You may also need to wear a physical activity monitor for 7 days.

Motor Skill We will measure your balance and coordination, which takes 10 minutes

Nutrition Assessment You will meet our dietitian who will ask you about the type of foods you eat to make sure you have the right food to help you grow. This will take 15-20 minutes

Fitness Your blood pressure will be taken and after this you will be given a heart-rate monitor to wear. You will then complete a walking test on a treadmill, which take 10-20 minutes.

Psychosocial Health You will meet Aoife, our team psychologist who will ask you to answer questions about the way you feel. This takes 20-30 minutes.

Timeline
You will do each of the tests listed above before and after the treatment (W82GO or smartphone application).

Duration
The project will take place over 12 months in total. You will need to come into the hospital with your parent(s) for measurements and/or treatment between 9 and 15 times during the study. If you decide not to do the study, you will still need to come to the hospital for the group programme.

QUESTION: *Can you tell me if you remember the number of times that you need to come to the hospital?? Do you have any questions?*
I have checked with the child and they understand that they will need to come into the hospital with their parents during the study period____(initial)

Risks: Is this dangerous for me?

The group treatment programme and smartphone application do not have any known side effects. However, we will follow you closely and keep track of you in case you have any problems throughout the study. We will give you a telephone number to call if you have questions. You can also come to the hospital to see me.

Will it hurt?

There are a few things that I want you to know. You have had a blood test before and know what that feels like. For the study you will have to have that once more at the end of the study. The blood test involves the placement of a needle in a vein in your hand or arm, which can cause a bruise or discomfort. We can use a special numbing medicine that will minimize the pain. Very rarely, a child may faint, or more likely become lightheaded when the needle is put in. The needle will be placed and removed while you are sitting or lying in bed in case dizziness does occur.

The fun exercise classes in the Group programme do not pose any extra risk to you. Although these classes will require physical effort, and are therefore tiring, this feeling is short-lived. You may have sore muscles after the classes but stretching and warm-up will help to minimize any discomfort.

QUESTION: *Do understand that we have not tested the smartphone application before? Do you understand that the blood test may hurt a little? Do you have any questions?*

I have checked with the child and they understand that the smartphone application has not been tested and that their follow up blood test might hurt____(initial)

Will the Study Help Me?

This study will help you. We will measure the amount of fat tissue in your body and will help you to reduce this. We will measure your fitness level which, will help you understand how fit you are and how you can become as healthy as possible. Overall, we hope the study will help us to learn more about how to treat children who are overweight in the best way possible.

Do I get anything for being in the study?

If you are in the smartphone group you will receive the smartphone application and phone for use over 12 months. If you are in the Healthy Lifestyles Programme Group you will receive phone only which you can use with your own phone service.

What if I Don't Want to be in the Study?

You should only participate in this research study if it is something you would like to do. Please feel free to say no. If you decide now that you want to participate but change your mind later, you may withdraw from the study at any time. These decisions will in no way affect your relationship with the doctors, nurses and researchers, or with the hospital.

QUESTION: *Do understand that if you take part you will receive a phone or phone plus phone service depending on the group that you are in? Do you have any questions?*

I have checked with the adolescent and they understand that if they participate in the study they will get a phone for use____(initial)

Confidentiality: Is my information safe?

The information that we collect from this research project will be put away and no-one but the researchers will be able to see it. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up with a lock and key. It will not be shared with anyone except the research team, hospital healthcare staff, and your doctor.
Information will be stored on password-protected computers, which are accessible only to members of our research team and those involved in managing the secure on-line database. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity.

- ***Question:*** *Did you understand the procedures that we will be using to make sure that any information that we as researchers collect about you will remain confidential? Do you have any questions about them?*

I have checked with the adolescent and they understand that if they participate their information will be stored securely ____(initial)

Will you tell me the results?

When you are finished the project, I will tell you about what we have learnt. I will also give you a paper with the results written down. Afterwards we will be able to tell more scientists and other what we found. We will do this by writing and sharing reports at meetings and in articles.

Who can I ask questions to?

Please ask questions at any time. You and your parents can talk to me or anyone else on the research team. If you wish to ask questions later, you may contact any of the following:
Grace O'Malley, physiotherapy Department, The Children's University Hospital, Temple Street, Dublin 1; Phone: 01 8784563; Email: grace.o'malley@cuh.ie

Principal Investigator: Grace O'Malley MSc MISCP

PART 2: Certificate of Assent

I have been invited to participate in research of obesity treatment at The Children's University Hospital.

I have read the foregoing information, or it has been read to me. I have had my questions answered and know that I can ask questions later if I have them.

I agree to take part in the research ☐

OR

I do not wish to take part in the research ☐ and I have not signed the assent below_____(initialed by child)

Only if child assents:

Print Name of Child_____

Signature of Child _____ Date _____Day/month/year

If illiterate
A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb print as well.

I have witnessed the accurate reading of the consent form to the child and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

*Print name of witness*_____ *AND* *Thumb print of parent*

Signature of witness _____ Date _____
Day/month/year

Statement by the researcher/person taking consent I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the child understands the study. I confirm that the child was given an opportunity to ask questions about the study and all the questions asked by him/her have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and that consent has been given freely and voluntarily.

A copy of this assent form has been provided to the participant ☐ _____ researcher initial)

Print Name of Researcher/person taking the assent_____
Signature of Researcher /person taking the assent _____
Date _____ Day/month/year

Parent/Guardian has signed an informed consent Yes ☐ No ☐ _____ researcher initial)

Smartphone user-agreement policy

CUH SMARTPHONE STUDY

The CUH smartphone study is intended for educational purposes and aims to help participants to make lifestyle changes in order to become as healthy as possible. Participants and their parents should read the information below so that they fully understand and agree to the conditions of the study.

Smartphone equipment

Parents are responsible for purchasing the smartphone (at a reduced cost) from the hospital for their child. They are also responsible for its safe-keeping. Whilst parents retain ownership and possession of the smartphone, they agree to grant to the mentors and hospital research team the right to collect and/or inspect the smartphone at any time and the right to alter, add, block or delete installed software or hardware. Participants may lose their right to use the smartphone service if they abuse their responsibilities and breach this agreement.

Substitution of Equipment

In the event that a participant's smartphone is inoperable, the hospital will try to provide a spare smartphone for use while the participant's smartphone is repaired or replaced. This agreement remains in effect for the substitute smartphone.

Damage or Loss of Equipment

Participants must report any damage or loss to their study mentor who will determine necessary action. All smartphones are covered by a manufacturer's warranty of one year. The warranty covers manufacturer's defects. If the smartphone is damaged by neglect or abuse, it is the family's financial responsibility to replace the smartphone.

Standards for personal smartphone care

Participant Responsibilities:

Follow your school's phone policy when in school.

Report any bullying, interference or intimidation by any other person to your parent and mentor

Read the information pack given to you around safe use of mobile phones and cyber bullying

Keep the smartphone in your school bag when not in use.

Do not let anyone use the smartphone other than your parents or guardians.

Adhere to this agreement at all times.

Report any problems, damage or theft immediately to your parent and mentor

Parental Responsibilities:

Read the information pack given to you around safe use of mobile phones and cyber bullying

Parents should inspect the smartphone each evening to ensure that it is in good working order.

Parents should report, immediately, any damage, interference or bullying relating to ownership, possession or use of the smartphone.

Parents should inspect the smartphone and the installed Apps on a regular basis to ensure that there is no inappropriate material on it or any inappropriate user.

Hospital's Responsibilities:

To enforce this agreement

To monitor usage of smartphone each month and report any inappropriate use to parents

General Care:

Do not do anything to the smartphone that will permanently alter it in any way.

Do not remove any serial numbers, identification or hospital labels placed on the smartphone.

Keep the equipment clean. For example, do not eat or drink while using the smartphone.

Screen Care

Clean the screen with a soft, dry anti-static cloth or with a screen cleaner designed specifically for LCD type screens only.

Personal Health & Safety

Avoid extended use of the smartphone while holding it to your ear. The smartphone can generate heat.

Take a 5 min break when using the smartphone for more than 15 minutes.

Do not provide your personal information to anyone over the Internet.

Keep the smartphone in a secure location.

Do not share your passwords with anyone.

Report any adverse events to your parents and the study mentor

If you see a message, comment, image, or anything else online that makes you concerned for your personal safety, bring it to the immediate attention of a teacher if you are at school or a parent / guardian if you are at home

Participants should never share personal information about themselves or others, including phone numbers, addresses, PPS numbers and birth-dates over the Internet without adult permission

Participants should never agree to meet someone they meet online in real life without parental permission.

Restricted Use and Confiscation

Participants who breach this agreement will be subject to restricted/limited access to the smartphone, at the mentor's discretion. Reasons for placing a participant on Restrictive Use include, but are not limited to the following:

Excessive damage

Excessive loss

Repeated failure to use hospital app

Repeated failure to attend hospital for scheduled appointments

Non-acceptance and/or compliance with this agreement

Inappropriate, defamatory, inaccurate, abusive, obscene, profane, or illegal material found on smartphone

Violating Standards for Personal smartphone Care

Failing to cooperate with investigations of abuse/or misuse of smartphone.

CUH online collaboration

CUH provides participants with messaging accounts for the purpose of study-related communication. Availability and use is restricted based on study policies.

Message usage may be monitored and archived.

CUH recognizes that online collaboration is essential to health-related learning. Participants are expected to communicate with one another in a safe, mindful and courteous manner.

All activity over the phone network will be monitored and may be retained

Access to online content via the network is restricted in accordance with this agreement

Participants are expected to respect that the web filter is a safety precaution, and should not try to circumvent it when browsing the Web.

Misuse of study resources will result in removal from the trial and disconnection of the phone service

We make a reasonable effort to ensure participants' safety and security online, but will not be held accountable for any harm or damages that result from misuse of study technologies

Participants are expected to alert his/her parent immediately of any concerns for safety or security

CUH Security

Participants are expected to take reasonable safeguards against the transmission of security threats over the study network. This includes not opening or distributing infected files or programmes and not opening files or programmes of unknown or un-trusted origin.

Use common sense if you think a website does not look right. Think twice before you click on anything you feel is not right.

If you believe the smartphone you are using might be infected with a virus, please alert your mentor.

Do not attempt to remove the virus yourself or download any programmes

to help remove the virus.

Participants should not download or attempt to download or run *.exe* programmes over the study network or onto study resources. You may be able to download other file types, such as images of videos if appropriate.

For the security of our network, download such files only from reputable sites, and only for educational purposes.

Netiquette

Netiquette may be defined as appropriate social behaviour over computer networks and in particular in the online environment. To this end

Participants should always use the Internet, network resources, and online sites in a courteous and respectful manner

Participants should also recognize that among the valuable content online is unverified, incorrect, or inappropriate content. Participants should use trusted sources when using the Internet

Participants should not to post anything online that they wouldn't want parents, teachers, or future colleges or employers to see. Once something is online, it is out there - and can sometimes be shared and spread in ways you never intended

More detailed examples of expected use and unacceptable use are given in Appendices One and Two.

Cyber-bullying

Harassing, flaming, denigrating, impersonating, outing, tricking, excluding and cyber-stalking are all examples of cyber-bullying.

Such behaviour will not be tolerated in the CUH study

Don't be mean. Don't send messages or post comments or photos with the

intent of scaring, hurting, or intimidating someone else

Engaging in any online activities intended to harm (physically or emotionally) another person, will result loss of privileges and exclusion from the study

In some cases, cyber-bullying is a crime

Remember that your activities are monitored and retained

The study will support participants, and parents in dealing with cyber-bullying as per CUH Child Protection procedures and will act as required by the *Department of Children and Youth Affairs*, *the Department of Justice and Equality* and the *Health Service Executive.*

Violations of this Expected Use Policy

Violations of this policy in CUH may have disciplinary repercussions, including:

Notification to parents in most cases

Suspension from study and/or study-related activities

Legal action and/or prosecution

We have read and understand the smartphone agreement and hereby agree to the terms of this agreement and grant to the study mentor and hospital authorities the right to inspect our child's smartphone and its Apps/programmes and in exceptional circumstances to confiscate it for a limited period because of abuse and/or misuse by either our child or any other person. We hereby agree and give permission to the hospital authorities to delete inappropriate material from our child's smartphone

and to prevent/block the installation of certain apps. We agree to be bound by the terms of this Policy, as they apply to ownership, possession and use of the smartphone and its installed apps.

I have discussed this Expected Use Policy with the study participant and guardian:

_____

(Study Principal Investigator, Printed Name)

_____

(Study Principal Investigator Signature)

_____

(Date)

I have read and discussed this Expected Use Policy with my child:

_____

(Parent / Guardian Printed Name)

_____

(Parent / Guardian Signature)

_____

(Date)

I have read and understood this Expected Use Policy and agree to abide by it:

(Participant Printed Name)

_____

(Participant Signature)

_____

(Date)

Examples of Expected Use

I will:

Use the study technologies for learning-related activities

Follow the same guidelines for respectful, responsible behaviour online that I am expected to follow offline.

Treat study resources carefully, and alert my parent/s and mentor if there is any problem with their operation.

Encourage positive, constructive discussion if allowed to use communicative or collaborative technologies.

Alert my parent and mentor if I see threatening/bullying, inappropriate, or harmful content (images, messages, posts) online.

Use smartphone at appropriate times, in approved places.

Recognize that use of the smartphone is a privilege and treat it as such.

Be cautious to protect the safety of others and myself.

Help to protect the security of the smartphone

This is not intended to be an exhaustive list. Participants should use their own good judgment when using study smartphones.

Examples of Unacceptable Use

I will not:

Use the smartphone in a way that could be personally or physically harmful to others or myself.

Search inappropriate images or content.

Engage in cyber-bullying, harassment, or disrespectful conduct toward others.

Try to find ways to circumvent the study's safety measures and filtering tools.

Use smartphone to send spam or chain mail.

Post personally identifying information, about others or myself.

Agree to meet someone I meet online in real life.

Use language online that would be unacceptable in the hospital or school.

Use smartphone for illegal activities or to pursue information on such activities.

Attempt to access sites, servers, accounts, or content that isn't intended for my use.

This is not intended to be an exhaustive list. Participants should use their own good judgment when using study technologies.

APPENDIX VIII.
TEMPLE STREET W82GO HEALTHY LIFESTYLES PROGRAMME MATERIALS

The W82GO! programme was established in 2005 by a multidisciplinary team. It is familbased and is delivered by a multidisciplinary team comprised of :

- Paediatrician
- Dietitian
- Nurse
- Chartered Physiotherapist
- Clinical Psychologist

W82GO provides families with health, nutrition, self esteem, family communication and activity guidance along with support in a safe environment so that families can achieve the healthiest lifestyle possible for them.

Proven Results:

Our team understands the specific medical and emotional needs of children and results have been successful to date.

Over the past three years, children who completed the W82GO! Programme improved their fitness levels and general health after one year.



Parents are required to attend each session with their children.

Parents learn to:

- Make positive changes in the family's lifestyle and communication patterns.
- Provide a balance between nurturing and limit setting.
- Act as positive role models for their children.

Children learn to:

- Create an active, full life where food and screen-time become less important as they have more fun being active.
- Communicate their needs in order to feel better about themselves.
- Make healthier lifestyle choices without feeling deprived/punished.

"W82GO! gave us the extra push we needed"

For further information call Sarah on 018921838



Temple Street W82GO! Healthy Lifestyles Programme



Temple Street
CHILDREN'S UNIVERSITY HOSPITAL

W82Go Final Leaflet.indd 1 14/01/2013 15:59:20



"The W82GO! Programme was excellent. My son's self esteem has greatly improved along with our eating habits"

Temple Street Children's University Hospital offers the W82GO! Healthy Lifestyles Program for children and teens, using a family approach. This programme helps families to create a home and lifestyle that promotes health. The programme is delivered by a multidisciplinary team of health professionals over 12 months:

Stage 1 takes place one evening per week for 6 weeks
Stage 2 involves 4 evening sessions (booster) 3-, 6-,9 and 12 months later

As this is a family based programme, parents/guardians are required to attend

Everybody is a different shape and size but nowadays more and more children have lifestyles that are not as healthy as they could be. Eating an unhealthy diet, not moving around enough (being inactive), not sleeping well and spending too much time using screens, can all have a negative effect on a child's health.

In Ireland, 17.8% of children aged 4-13 years are described as overweight and 6.8% as obese. In some cases being overweight can indicate that a child may be at risk of illnesses such as asthma, type 2 diabetes and heart disease. In other cases children who are overweight may experience joint pain, high blood pressure, low self esteem, or depression and are at greater risk of becoming an overweight adult.

Where does W82GO! take place?

- The programme runs on Thursday evenings between 5.30 and 7.30pm in the hospital.
- Children should wear comfortable clothes and runners and bring a bottle of water with them.

What happens on the programme?

- Every week both children and parents take part in practical education sessions.
- Children also take part in 60 minutes of fun, group based activity with children their own age in a safe and encouraging environment

How can our family take part?

- Before your family takes part in the programme, your hospital doctor will request a FASTING blood test to measure levels of insulin, lipids, and blood sugar.
- Before starting the programme you will be required to attend the hospital for a screening appointment by the team.

Screening Visit

- This appointment will include: a dietary assessment, a fitness test (heart, lungs, muscles and joints) and questionnaires regarding the sleep pattern, quality of life and emotional wellbeing of your child.
- This assessment will give us important information about your child's risk of illness and family medical history. Using this comprehensive assessment, we will draw up an individual plan.

W82GO Healthy Lifestyles Service referral form

Temple Street CHILDREN'S UNIVERSITY HOSPITAL | 140 YEARS Caring for Sick Children

W82GO

Referral to Temple Street W82GO Healthy Lifestyles Programme

Children >98th percentile for BMI only

The following information is mandatory in order for the child to be assessed for the programme.

Name:	**D.O.B:**
Address:	
Parent/s Name:	**Parent Contact**

Dear Dr. Sinead Murphy,

Thank you for kindly assessing the above patient for his/her suitability to attend the Temple Street W82GO! Programme.

Date of Assessment:		**Gender**	
Height (cm)		**Weight (kg)**	
BMI		**Waist circumference**	
Referral discussed with child's parents	**YES ☐ NO ☐ If No, Why not?**		
Blood pressure			
Evidence of hypothyroidism?			
Cutaneous markers?			
Symptoms of diabetes?			
Other Information			

I accept that this information is intended as a guideline only.

Yours sincerely,

Clinician Signature **Clinician Phone No.** **Date of Referral**

W82GO Clinical assessment form

Children's University Hospital
TEMPLE STREET, DUBLIN

W82GO! ASSESSMENT

Name:

HRN:

Referral Date *By: GP ☐ CUH Consultant ☐ Other ☐* *Referral Weight* *Referral Height* *Referral BMI*	**Clinician** *Name* *Signature*	**Assessment Date** **Child Accompanied** *By: Mum ☐ Dad ☐ Other ☐*
Does parent know why they are here? *Whose idea was it to come?*		
Social History *Who lives at home?* *School and class/year* *Missing school?* YES ☐ NO ☐ WHY?	**Birth History** *Birth Weight:* *Gestational Age:* /40 *Gestational diabetes* YES ☐ NO ☐ *Breast-fed* YES ☐ NO ☐ How many months? *Difficulties weaning?*	
Child Medical/surgical History	*Learning Difficulties* YES ☐ NO ☐ What *Development* NORMAL ☐ DELAYED ☐ HOW?	
Mental/emotional health *Behavioural difficulties* YES ☐ NO ☐ What *Emotional health problems* YES ☐ NO ☐ What *Is child linked with mental health professional* YES ☐ NO ☐ Details		
Family Medical History *CVD* YES ☐ NO ☐ WHO *Hypertension* YES ☐ NO ☐ WHO *Thyroid* YES ☐ NO ☐ WHO *Diabetes(1/2)* YES ☐ NO ☐ WHO *Stroke* YES ☐ NO ☐ WHO *Overweight* YES ☐ NO ☐ WHO		**Medications** **Allergies**
Weight trajectory *Age when first bigger than peers:* *Is weight? stable ☐ increasing ☐ decreasing ☐* *Has child seen someone before regarding weight?* YES ☐ NO ☐ WHO *Have changes been made already?* YES ☐ NO ☐ IF YES, WHAT / IF NO, WHY?		

Anthropometry	**Date**
Weight (kg) / Centile	*BMI*
Height (cm) / Centile	*BMI Centile*
Waist Circumference (cm)	*BMI SDS*
Percent Fat	*Lean Mass*

Examination	
Striae *(colour and location)* *Acanthosis nigricans* *Neck* ☐ *Axilla* ☐ *Elbows* ☐ *Wrists* ☐ *Hirsute* ☐ *Acne* ☐ *Goitre* ☐ *Wheeze* ☐ *Fat Deposit Centralized* ☐ *Generalized* ☐	*Blood pressure* ***Syndrome-related** *Hypogonadism* ☐ *Deaf* ☐ *Hair colour* ☐ *Dysmorphic Features:*

Comorbidities		
Function	*Problems with any day to day activities because of weight (e.g tying shoes; showering)?* *Incontinence (day-time or night-time)?*	
Breathing	*SOB at rest* ☐ *Walking up stairs* ☐ *Walking 100m* ☐ *Doing the same things as peers* ☐	
Orthopaedic ***LIMP=outrule SUFE**	*Pain Low back* ☐ *Hips* ☐ *Knees* ☐ *Feet* ☐ *Other* ☐ *Other limitation (gait, Malalignment)* *Previous fracture?* YES ☐ NO ☐ WHAT	
Sleep **Fill out Sleep disorders scale if appropriate	*Hours on school night* *Hours on weekend night* *Difficulty getting to sleep?* *Waking during night?*	*Snoring* YES ☐ NO ☐ *Apnoea* YES ☐ NO ☐ *Breathing difficulties* YES ☐ NO ☐
Endocrine	**Diabetes** *Polydypsia* YES ☐ NO ☐ *Polyurea* YES ☐ NO ☐ *Puberty started yet?* YES ☐ NO ☐ *Age of menarche*	**Girls only** *Hx significant acne? Back* ☐ *Face* ☐ *Chest* ☐ *Hirsute* ☐ *Hair control?* *Duration of cycle* *Heavy periods? School days missed?*

Eating Behaviour

Have you made changes to what you and your child eat at home in the past year? YES ☐ NO ☐ WHAT ☐

How often to you sit down to eat together *Never* ☐ *Sometimes* ☐ *Most days* ☐ *Everyday* ☐

Do you/parent read food labels YES ☐ NO ☐ *Do you have access to a full supermarket* YES ☐ NO ☐

How much milk per day (mls) *Other dairy products/sources of Ca+?*

Does child eat while watching TV/using computer YES ☐ NO ☐ *Does child hide food* YES ☐ NO ☐

Does child ever eat at night YES ☐ NO ☐ *Does child ever feel full* YES ☐ NO ☐

When child starts eating does he/she keep eating even though full? YES ☐ NO ☐

How often does child have

	Daily	*>5 /7*	*>2 /7*	*Never*	*What do you usually have?*	*Where?*
Breakfast						
Lunch						
Dinner						

	Times per week		*Times per week*		*Times per week*
Sugary cereals		*Flavoured Milk*		*Take Aways*	
Breakfast rolls		*Plain bix*		*Ready meals*	
Sugar in tea/cereal		*Crisps*		*Pizzas*	
Fruit juice (fresh)		*Chocolate bix*		*Nuts*	
Chips		*Fizzy drinks*		*Ice cream*	
Ice pops		*Fruit juice (in carton/pack)*		*Sports drinks*	

Does child eat more when: Happy: YES ☐ NO ☐ Lonely: YES ☐ NO ☐ Bored: YES ☐ NO ☐
Angry YES ☐ NO ☐ Sad YES ☐ NO ☐ Upset YES ☐ NO ☐

Physical Activity ***Complete PAQ-C/ PAQ-A*

Do you consider your child to be physically active YES ☐ NO ☐ WHY ☐

Is child getting recommended 60 mins of PA (that makes them breathe hard) everyday? YES ☐ NO ☐ WHY ☐

Hours per week in PE *Hours per week in planned activity (details)*

How does child get to school? *Is walking/cycling to school possible?*

Does child have: bike ☐ scooter ☐ trampoline ☐ back garden ☐ safe place to play ☐ Wii ☐ Kinect ☐
Barriers to becoming more physically active (detail)

Sedentary pursuits

Does child do mostly inactive things in free time? YES ☐ NO ☐

Hours of TV on school day *Hours of TV weekend day*

Hours of computer/laptop on school day *Hours of computer/laptop weekend day*

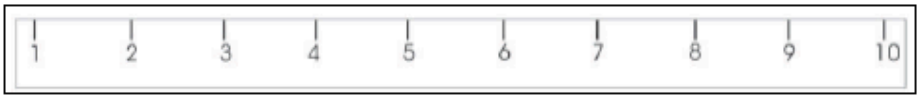
Hours of phone/texting on school day *Hours of phone texting weekend day*

Readiness to Change

Concerned about child's weight? *Parent* YES ☐ NO ☐ Child YES ☐ NO ☐

Has child been teased because of weight? YES ☐ NO ☐ By WHOM?

How ready are YOU to make changes for the benefit of their child's health



Not Ready *Unsure* *Ready*

Do you think it will be possible to move towards 10? YES ☐ NO ☐

Do parent or child have any concerns about making changes (detail)?

Investigations/onward referral ** Cholesterol; HDL; LDL; Trig; Glucose; HbA1C ; Insulin; Liver Fxn ; CRP;*

Bloods ***W82GO bloods**** ☐ *Thyroid Fxn* ☐ *Vit D* ☐ *Bone Profile* ☐ *Genetic screen* ☐

OGTT ☐ *Pelvic Ultrasound* ☐ *ECG* ☐ *24 blood pressure /cardiology* ☐

Summary

Problem List	*Short-term goals*	*W82GO Booklet given* ☐
1		
2	*1*	*Bloods ordered* ☐
3	*2*	
4	*3*	***Interested in returning for treatment:*** NO ☐ *Why?*
5		
		➔ *DC letter to referrer/GP/parent*

Interested in returning for treatment: YES ☐ *Appropriate for group programme?* YES ☐ NO ☐

If YES ➔ *Referral to Psych* ☐ *Add to group list* ☐ *12-month RV apt* ☐ *If No* ➔ *3-month RV apt* ☐

If 12 or over, interested in smartphone study? ➔ *Study info leaflet given* ☐ *Exercise test arranged* ☐