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Title	The development and implementation of targeted dietetic interventions during cancer survivorship, with a focus on early-stage, hormone-receptor positive breast and gynaecologic cancers
Authors	Johnston, Katie
Publication date	2026-02-13
Original Citation	Johnston, K. E. 2026. The development and implementation of targeted dietetic interventions during cancer survivorship, with a focus on early-stage, hormone-receptor positive breast and gynaecologic cancers. PhD Thesis, University College Cork.
Type of publication	Doctoral thesis
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Download date	2026-10-25 14:12:57
Item downloaded from	https://hdl.handle.net/10468/19313

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The Development and Implementation of Targeted Dietetic Interventions During Cancer Survivorship, with a Focus on Early-Stage, Hormone-Receptor Positive Breast and Gynaecologic Cancers

Thesis presented by

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For the degree of

Doctor of Philosophy

University College Cork

School of Food and Nutritional Sciences

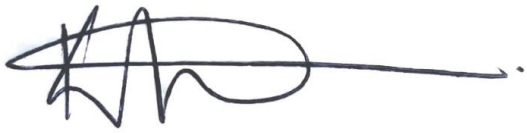
Head of School: Professor Alan Kelly

Supervisors: Dr Samantha Cushen and Professor Aoife Ryan

2026

DECLARATION

This is to certify that the work I am submitting is my own and has not been submitted for another degree, either at University College Cork or elsewhere. All external references and sources are clearly acknowledged and identified within the contents. I have read and understood the regulations of University College Cork concerning plagiarism and intellectual property.



Katie E Johnston

13th February 2026

Date

ACKNOWLEDGEMENTS

This thesis would not have been possible without the contribution, support and guidance of many.

First and foremost, I would like to thank my supervisors, Dr Samantha Cushen and Professor Aoife Ryan. Samantha – you have made this journey such an enjoyable experience. Thank you for your supportive words, your encouragement and your guidance – and for finding a way to make my many research ideas become a reality. You have created an environment where I constantly feel energised by the research we conduct. I am indebted to you for the many opportunities that you have provided me with over the last number of years. It has been a privilege to learn from you and work alongside you. You are an advocate for your students and people affected by cancer, who are often forgotten about. I look forward to continuing to work with you in the future to innovate and improve dietetic care for those that need it most. Prof Aoife Ryan, thank you for responding to that email back in May 2021 and welcoming me into your research group. It has been a privilege to work with and learn from such a leader in the field - thank you for your kindness, guidance and support.

To Professor Roisin Connolly and Professor Josephine Hegarty, it has been a privilege to work with you on the LYSA Trial. I am extremely grateful to have worked side by side with such innovators and advocators for change. Thank you for keeping a seat at the table for dietitians and understanding the necessity of our service. For the opportunities you have afforded me, both on the LYSA Trial and beyond. I hope to continue to work with you in the future and change the care for our patients for the better.

To Ms Kate O'Connell and Ms Naoimh Flynn – you both took me under your wing back in August 2022, where I have stayed! It has been a pleasure and a privilege to work with and learn from such knowledgeable nurses who I now call good friends. Our healthcare community and patients are lucky to have you. Thank you for always finding the light and helping me to find it too – especially in Room 25!

To all the staff in Orchid Centre and the oncology dietitians in Cork University Hospital – Gillian, Elaine, Aislinn and Sarah, (to name a few!), your positivity and warm smiles in an unbelievably busy environment have never failed to give me a boost. To Dr Fiona Byrne, Dietitian Manager at Cork University Hospital – thank you for advocating for dietetic research and researchers.

To Ms Jette Verde and Mr Jonathan Leahy Maharaj – thank you for bringing *Menopause, Diet and Cancer* to life. You have created a beautiful book that has those who need it most at the centre and crafted it with true care, expertise and dedication.

To our review panel – Dr JJ Keating, Ms Sorcha Ryan, Ms Yvonne O'Meara, Ms Doireann Ni Chonaill, Ms Ciara O'Connor, Dr Elaine McCarthy, Mx Ryan Goulding – thank you for your expertise, and contribution to *Menopause, Diet and Cancer.*

To Dr Brendan Palmer and Dr Darren Dahly – thank you for your statistical guidance, patience and good humour throughout the LYSA Trial.

To Dr Laia Raigal and the team at Cancer Research @UCC, particularly, Prof Jack Gleeson, Dr Brendan Noonan and the LIAM Mc Team – thank you for all the opportunities that you have afforded to me, and for recognising the strength of multi-disciplinary teams. To the BSc and MSc students of School of Food and Nutritional Sciences – thank you for your contribution to this research.

To the Irish Cancer Society and Breakthrough Cancer Research - the funding you have provided for survivorship research will work to change the standard of care throughout Ireland. Thank you for acknowledging the vital role of dietitians. A particular thanks to Ms Veronica McSharry, Dr Niki Warner, Ms Aanya Sagheer, Dr Claire Kilty, Ms Amy Nolan and Ms Orla Dolan for their continued support in creating and championing resources for people affected by cancer.

To the NCCP Alliance Cancer Support Centres, the charities and the organisations who assisted in disseminating this research – thank you and thank you for the work you do for all those affected by cancer in this country.

To my parents, Moya and Mal. Your hard work and sacrifices have given me so many opportunities, including my education, that are not afforded to others. I want to sincerely thank you. Your support and encouragement, and endless *FaceTime*s, has meant so much to me, and kept me going! You have always championed me, and I am so lucky for that.

Holly – thank you, for every word of encouragement and phone call, for your well-timed humour and perspective that I needed throughout this journey. You have been my rock, and I am so grateful to have a sister like you by my side. I couldn't have done this without you.

A PhD becomes your whole world, and I am very lucky to be surrounded by such a gorgeous community who are always in my corner. Annie, Harriet, Megan, Aislinn, Julie, Ciara, Skye, Tara, Allie, Hannah and Lizzie - thank you for cheering me on every step of the way, it means more than you all know.

Alan – your calm, constant encouragement and well-timed reminders to occasionally step away from my laptop and go outside has made the final stretch much easier. Your confidence in me, particularly when my own waivered, kept me going. Thank you, it has meant the world to me.

To Mr Damien Courtney – thank you for your guidance, and the time you have taken to ensure this work was perfect. A true academic, and I hope to have a career as fulfilling and as prosperous as yours.

To Dr Lizzy Deery and Dr Tom Butler – thank you for opening the research door for me at the University of Chester and encouraging me down this path. I thoroughly enjoyed my first research experience, and it was thanks to you both. Conducting my BSc Thesis, I was extremely moved by the experiences of women, particularly those in the Southwest of Ireland, where I have found myself. It feels a little full circle.

Most importantly, to every woman who participated in this research over the past 3 years – thank you, sincerely. To the "*What Women Want*" Focus Group participants, your discussions were candid, thought-provoking, and importantly, practice changing. You have laid the foundations for future dietetic services for women who are often forgotten about – I am most grateful for the generous time and insights you have contributed.

To the LYSA Trial participants - thank you for your openness, honesty and vulnerability during this part of your journey, on the good days and the bad. It has been my privilege to get to know and support you during your time with us. It is not lost on me how much courage it takes to enter into the unknown of a clinical trial and trust us with your care during this time. From the bottom of my heart, thank you.

You have paved the way for all who will follow your footsteps – go n-éirí an bóthar libh.

THESIS SUMMARY

The global incidence of cancer has increased over the last decade, and due to advances in treatment and early detection, the number of survivors living with and beyond a cancer diagnosis is rising. Women surviving early-stage breast and gynaecologic cancers often experience complex supportive care needs, including alterations in body composition, increased risk of chronic disease, and long-term symptoms associated with medically induced (iatrogenic) menopause. Despite evidence suggesting that dietitian-led interventions are feasible and valued by survivors, structured survivorship services in this population remain limited. Contributing factors include resource constraints, fragmented care pathways, and insufficiently tailored nutritional screening and intervention strategies. In the absence of formal support, many survivors take control of their own health through complementary and alternative approaches, including dietary and herbal supplements, often without professional guidance. Emerging literature underscores both the potential benefits of patient-centred dietetic care and the substantial gaps in nutritional guidance, screening, and supplement management that persist for breast and gynaecologic cancer survivors.

The primary aim of this thesis was to explore the feasibility and acceptability of a dietitian- and nurse-led survivorship clinic using electronic patient-reported outcomes and evaluate the impact of a dietitian-led intervention on nutrition-specific needs, body composition, dietary quality, weight gain concern, and psychosocial outcomes in women surviving early-stage breast and gynaecologic cancers. The thesis further aimed to investigate the prevalence, motivations, and information sources of dietary and herbal supplement use in female cancer survivors affected by iatrogenic menopause, identifying gaps in professional guidance. Finally, it sought to develop,

co-design, and implement a multimodal, symptom-responsive dietary resource tailored to survivors' nutritional and symptom-management needs, assessing its reach, engagement, and utility for both survivors and healthcare professionals.

The Linking You to Support and Advice (LYSA) Randomised Controlled Trial and its complex intervention utilising ePROs proved to be feasible among 200 participants and highly acceptable to participants and healthcare professionals through its concurrent process evaluation. Findings suggested that a bi-monthly supportive care intervention can significantly improve fatigue, anxiety, depression and health-related quality of life scores, as well as significantly reducing patient-reported weight gain concern when compared to an active comparator. Importantly, despite improvements in psychosocial outcomes, the research highlighted that current nutritional screening tools and guidelines lack specificity, failing to capture the nutritional considerations and risks faced by this cohort, moving beyond traditional malnutrition concerns.

This thesis also explored dietary and herbal supplement use among female cancer survivors affected by iatrogenic menopause. Supplement use was highly prevalent, including widespread poly-supplementation and frequent use of herbal products outside recommended guidelines. Motivations for supplement use were largely symptom-driven, yet healthcare professionals, including dietitians, were infrequently consulted, with survivors relying heavily on digital and social media sources for guidance. These findings revealed gaps in professional advice and emphasised the need for structured, evidence-based interventions to support safe and effective supplement use, particularly for managing fatigue, vasomotor symptoms, musculoskeletal pain, and cognitive changes.

In response to these gaps, a co-designed, multimodal dietary resource was developed to address survivors' nutritional and symptom-management needs. The *Menopause Plate* © dietary model through the *Menopause, Diet and Cancer* resources provided practical, evidence-informed guidance for managing common menopause-related symptoms while bridging self-directed behaviours with professional support. Engagement with the resource was substantial (n = >12,500), with wide dissemination through printed booklets, webinars, and online materials.

Collectively, this thesis demonstrates that symptom-responsive, dietitian-led care is feasible, acceptable, and potentially impactful for women surviving breast and gynaecologic cancers. Structured interventions, combined with digital tools and co-designed dietary resources, offer a foundation for patient-centred survivorship care that improves psychosocial outcomes, supports informed nutritional decision-making, and enhances quality of life. The research presented in this thesis establishes a framework for future practice, highlighting the need for refined nutritional screening tools, structured guidance on supplement use, and strategies to ensure equitable, scalable implementation of dietetic interventions across survivorship pathways.

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STATEMENT OF CONTRIBUTION

This thesis comprises eight chapters, including a series of studies derived from a multicentre clinical trial.

Trial Background

The clinical trial underpinning Chapters 2 to Chapter 5 was designed and granted ethical approval in December 2020. Recruitment ran from March 2021 to August 2022. The candidate joined in September 2022, prior to commencing doctoral studies in January 2023, and subsequently assumed major leadership responsibilities. Contributions included management of dietetic components at two trial sites, data collection, delivery of the dietetic intervention, data analysis and interpretation, and preparation of the trial dietetic protocol for scientific publication.

Candidate Contributions

Chapter 2

The candidate drafted the trial dietetic protocol for scientific publication, which described the intervention, research questions, and data management procedures. This work established the framework for the trial, including the structure of dietetic assessments, use of ePROs, and planned analyses.

Chapter 3

The candidate contributed to the delivery of the intervention at one study site and oversaw the delivery at the second site, collected participant data relevant to the feasibility outcomes, and drafted the paper for publication. Statistical analyses were performed in collaboration with Dr. Darren Dahly (Study Principal Biostatistician), with the candidate contributing to the analysis plan, interpretation of findings, and integration of results. The chapter was drafted and revised to ensure clarity and coherence.

Chapter 4

The candidate developed the research questions, delivered the intervention, collected the data, curated and interpreted the dataset, performed all statistical analyses, and drafted and revised the chapter.

Chapter 5

The candidate developed the research questions, delivered the intervention, collected the data, curated and interpreted the dataset, performed all statistical analyses, and drafted and revised the chapter.

Chapter 6

The candidate designed the protocol and questionnaire, developed the research questionnaires, recruited participants, collected data, curated and interpreted the dataset, performed all statistical analyses, and drafted and revised the chapter.

Chapter 7

The candidate conceptualised the design of the multi-modal resource and conducted the literature review, undertook the nutritional analyses and recipe testing, developed and delivered the webinar series, developed the contents of the book and actively disseminated the resources, and drafted and revised the chapter.

Authorship and Responsibility

All chapters included in this thesis were written by the candidate.

Co-authors provided feedback, editorial input, and domain-specific expertise as appropriate. The candidate takes responsibility for the coherence of the thesis as a whole and for the interpretation of results presented.

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LIST OF ABBREVIATIONS

24HR	24 hour
AC	Active Comparator
BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
CI	Confidence Intervals
DNA	Did Not Attend
DFS	Disease Free Survival
E	Experimental
ECOG	Eastern Cooperative Oncology Group
EDC	Electronic Data Capture
EORTC	European Organisation for Research and Treatment of Cancer
EPIC	European Prospective Investigation into Cancer
ePROs	electronic Patient Reported Outcomes
FFQ	Food Frequency Questionnaire
FU	Follow Up
g	grams
GP	General Practitioner
HBS	Herbal Botanical Supplements
HCP	Healthcare Professional
HGS	Handgrip Strength
HOMA-IR	Homeostatic Model Assessment for Insulin Resistance
HRQOL	Health Related Quality of Life
IT	Information Technology
IQR	Interquartile Range
Kcal	kilocalories
kg	kilograms
kg/m^2	kilogram per metres squared
lbs	pounds
LYSA	Linking You to Support and Advice
MDT	Multidisciplinary Team
MedD	Mediterranean Diet

mg	micrograms
MST	Malnutrition Screening Tool
NIH-AARP	National Institutes of Health American Association of Retired Persons
NPAQ	Nordic Physical Activity Questionnaire
ORs	Odds Ratio
PCN	Personalised Nutritional Counselling
PG-SGA	Patient-Generated Subjective Global Assessment
PP	percentage point
PPI	Patient and Public Involvement
PRO-CTCAE	Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events
PROMIS	Patient-Reported Outcomes Measurement Information System
QoL	Quality of Life
RCT	Randomised Controlled Trial
RD	Registered Dietitian
SD	standard deviation
VMS	Vitamin and Mineral Supplements
WCRF	World Cancer Research Fund
WCRF/AICR	World Cancer Research Fund/American Institute for Cancer Research
WGC	Weight Gain Concern

TERMINOLOGY:

For the purpose of this thesis, the term "cancer survivor" is defined as someone who has completed active cancer treatment, including chemotherapy, radiotherapy and/or surgery.

LIST OF PUBLICATIONS AND SCIENTIFIC CONFERENCE PRESENTATIONS ARISING FROM THIS WORK

Scientific Publications

Peer-Reviewed Journals

The Breast

- **Johnston K.E**, O'Connell K., Raigal-Aran L., et al. A complex survivorship intervention utilizing electronic patient-reported outcomes in breast and gynecologic Cancer: the linking you to support and advice [LYSA] trial. Breast. 2026;86:104740. doi:10.1016/j.breast.2026.104740

Proceedings of the Nutrition Society

- Keaver, L., O'Callaghan, N., **Johnston, K. E.**, & Cushen, S. J. (2026). Nutrition in cancer survivorship: bridging the evidence-practice gap. Proceedings of the Nutrition Society, 1–12. doi:10.1017/S0029665125102152

HRB Open Research

- **Johnston, K. E.**, O'Connell, K., McSharry, V., et al. (2025). A Dietitian Survivorship Clinic For Early-Stage Breast and Gynaecologic Cancer Survivors: A Dietetic Protocol For The Linking You To Support And Advice (LYSA) Randomised Controlled Trial (Version 1; peer review: awaiting peer review). HRB Open Research, 8, 77. https://doi.org/10.12688/hrbopenres.14187.1

BMC Research Involvement and Engagement

- Medved, K., **Johnston, K.E.**, Thomas, S. S., et al. (2025). Patient and public involvement in randomised controlled trial design and implementation: A process evaluation of the Linking You to Support and Advice (LYSA) trial. Research Involvement and Engagement, 11, 74. https://doi.org/10.1186/s40900-025-00746-8

Clinical Nutrition Open Science

- Cushen, S. J., Murphy, M., & **Johnston, K. E.** (2025). "What women want": Focus group discussions to inform the design of nutrition resources for women impacted by menopause following cancer treatment. Clinical Nutrition Open Science, 59, 189–205. https://doi.org/10.1016/j.nutos.2024.12.006

The Boolean Journal

- **Johnston, K. E.,** Ryan, A., & Cushen, S. J. (2024). Nutrition for female menopausal cancer survivors: Developing Ireland's first resource. The Boolean Journal, 7. https://doi.org/10.33178/boolean.2024.1.27

Non-Peer-Reviewed Journals

Hospital Professional News

- **Johnston, K. E.,** & Cushen, S. J. (2025). The forgotten patients: Why does the supportive care stop? Hospital Professional News, 128, 68–72.

Complete Nutrition Professional Magazine

- **Johnston, K. E.,** Ryan, A., & Cushen, S. J. (2023). The role of a dietitian in the survivorship stage of the cancer care pathway: Novel or necessary? The Women's Health Initiative LYSA (Linking You with Advice and Supports) Trial. Complete Nutrition Professional Magazine. Wiley Publications.

Cancer Professional Magazine

- Cushen, S. J., & **Johnston, K. E**. (2024). Navigating menopause after cancer: Unique nutritional challenges for female survivors. Cancer Professional Magazine.

Books

- **Johnston, K. E**., & Cushen, S. J. (2025). Menopause, diet & cancer: Eating well after cancer. School of Food and Nutritional Sciences, University College Cork. https://www.cancer.ie/menopauseplate

Webinar Series

The Irish Cancer Society

- **Johnston, K. E.,** & Cushen, S. J. (2024). Menopause, Diet and Cancer [Webinar series]. YouTube. https://tinyurl.com/menodietcancer

Oral Presentations at Scientific Conferences

San Antonio Breast Cancer Symposium

- **Johnston, K. E.,** O'Connell, K., Flynn, N., McSharry, V., Raigal-Aran, L., Ryan, A. M., Palmer, B., Dahly, D., Hegarty, J., Cushen, S. J., & Connolly, R. M. (2025). Impact of a dietitian and nurse-led survivorship clinic utilizing ePRO collection on body composition and muscle strength in early-stage breast cancer: Results from the Linking You to Support and Advice (LYSA) randomized control trial [Conference abstract]. San Antonio Breast Cancer Symposium, San Antonio, TX. https://doi.org/10.1158/1557-3265.SABCS24-PS15-04

American Society of Clinical Oncology

- O'Connell, K., Raigal-Aran, L., **Johnston, K. E**., Cushen, S. J., Flynn, N. M., O'Reilly, S., Collins, D. C., Noonan, S., Cleary, V., Kearns, N., Medved, K., Davis, A., Byrne, F., Dahly, D. L., Palmer, B. A., Murphy, A., McInerney, V. B., Lowery, A. J., Hegarty, J., & Connolly, R. M. (2024). Evaluation of a complex survivorship intervention incorporating electronic patient-reported outcomes in early-stage breast and gynaecologic cancer: Results from the LYSA randomized controlled trial. Journal of Clinical Oncology, 42(16 Suppl), 1505. https://doi.org/10.1200/JCO.2024.42.16_suppl.1505

Academic Poster Presentations at Scientific Conferences

European Society of Medical Oncology Gynaecological Cancer Congress (2025)

- Medved, K., **Johnston, K. E**., Raigal-Aran, L., Hegarty, J., Connolly, R. M., & O'Connell, K. (2025). Patient and public involvement (PPI) in randomised controlled trial design and implementation: A process evaluation of the Linking You to Support and Advice (LYSA) trial [Poster presentation].

European Society of Medical Oncology Gynaecological Cancer Congress, Vienna, Austria.

Irish Nutrition and Dietetic Institute Research Symposium (2025)

- **Johnston, K. E**., Larkin, S., & Cushen, S. J. (2025). The use of dietary supplements to alleviate menopausal symptoms in female cancer survivors [Poster presentation]. INDI 10th Research Symposium, Dublin, Ireland.
- **Johnston, K. E**., McSharry, V., Ryan, A. M., Sagheer, A., Warner, N., & Cushen, S. J. (2025). Addressing nutritional gaps for women affected by cancer: The Menopause, Diet and Cancer webinar series [Poster presentation]. INDI 10th Research Symposium, Dublin, Ireland.
- **Johnston, K. E**., O'Connell, K., Raigal-Aran, L., Ryan, A. M., Dahly, D., Hegarty, J., Connolly, R. M., & Cushen, S. J. (2025). A dietitian-led medical oncology outpatient clinic for early-stage breast cancer survivors focused on weight gain concern and body composition: Results from the LYSA randomised control trial [Poster presentation]. INDI 10th Research Symposium, Dublin, Ireland.

European Society of Menopause and Andropause (2025)

- **Johnston, K. E**., Larkin, S., & Cushen, S. J. (2025). Alleviating menopausal symptoms: The use of dietary and herbal supplements in Irish cancer survivors impacted by menopause [Poster presentation]. European Society of Menopause and Andropause, Valencia, Spain.

Irish Society of Clinical Nutrition and Metabolism (IrSPEN) (2025)

- **Johnston, K. E**., O'Connell, K., Hegarty, J., Collins, D., Ryan, A. M., Connolly, R. M., & Cushen, S. J. (2025). Are cancer survivors falling through the gaps? A case study in multidisciplinary services for gynaecologic cancer survivors [Poster presentation]. IrSPEN Annual Meeting, Dublin, Ireland.
- **Johnston, K. E**., O'Connell, K., McSharry, V., Ryan, A. M., Hegarty, J., Connolly, R. M., & Cushen, S. J. (2025). Exploring dietary and herbal supplement use in early-stage breast and gynaecologic cancer survivors [Poster presentation]. IrSPEN Annual Meeting, Dublin, Ireland.

Menopause Society of Ireland (2024)

- **Johnston, K. E.,** & Cushen, S. J. (2024). The Menopause Plate: A dietitian-led initiative to support female cancer survivors [Poster presentation].

European Society of Clinical Nutrition and Metabolism (ESPEN) (2024)

- **Johnston, K. E.**, McSharry, V., Davis, A., Bermingham, K., Byrne, F., Raigal-Aran, L., O'Connell, K., Flynn, N. M., Palmer, B. A., Dahly, D. L., Lowery, A. J., Ryan, A., Hegarty, J., Connolly, R. M., & Cushen, S. J. (2024). Examining the feasibility of a dietetic intervention on body composition in Irish breast and gynaecological cancer survivors: The LYSA trial [Poster presentation].

American Society of Clinical Oncology (2024)

- Ghassemi Rad, M. J., O'Connell, K., Raigal-Aran, L., **Johnston, K. E**., Flynn, N. M., O'Reilly, S., Noonan, S., Medved, K., McInerney, V. B., Lowery, A. J., Palmer, B. A., Dahly, D. L., Hegarty, J., & Connolly, R. M. (2024). Assessment of endocrine therapy adherence in a nurse-led cancer survivorship clinic: Results from the LYSA trial [Poster presentation]. Journal of Clinical Oncology, 42(16 Suppl), 1627. https://doi.org/10.1200/JCO.2024.42.16_suppl.1627

Irish Psycho-Social Oncology Network (IPSON) Conference (2024)

- O'Connell, K., **Johnston, K. E**., Flynn, N. M., Raigal-Aran, L., Cushen, S. J., Medved, K., Dahly, D. L., Palmer, B. A., Hegarty, J., & Connolly, R. M. (2024). The Women's Health Initiative Linking You to Support and Advice (LYSA): A patient-guided multi-disciplinary survivorship trial [Poster presentation]. IPSON Annual Conference, Dublin, Ireland. (Co-first authors.)

Irish Association for Cancer Research (2024)

- **Johnston, K. E.,** Murphy, M., & Cushen, S. J. (2024). Designing nutrition resources for women affected by menopause post-cancer treatment: Insights from "What Women Want" focus groups [Poster presentation].

European Society of Clinical Nutrition and Metabolism (ESPEN) (2023)

- **Johnston, K. E.,** Cushen, S. J., Davis, A., Bermingham, K., O'Grady, A., Byrne, F., O'Connell, K., Flynn, N. M., Raigal-Aran, L., Dahly, D. L., Palmer, B. A., Connolly, R. M., & Hegarty, J. (2023). Developing the use of electronic patient-reported outcomes to implement dietetic intervention for a pilot survivorship clinic for women diagnosed with breast and gynaecological cancer in Ireland: The Women's Health Initiative LYSA study [Poster presentation]. https://doi.org/10.1016/j.clnesp.2023.09.120
- Murphy, M., **Johnston, K. E.,** & Cushen, S. J. (2023). "What Women Want": Focus group discussions to inform the design of nutrition resources for women impacted by menopause following cancer treatment [Poster presentation]. https://doi.org/10.1016/j.clnesp.2023.09.574

Irish Society of Clinical Nutrition and Metabolism (IrSPEN) (2023)

- **Johnston, K. E.,** Flynn, N. M., O'Connell, K., Connolly, R. M., Ryan, A. M., & Cushen, S. J. (2023). "The Oars to Help You Paddle": Oncology-Acquired Recovery and Support – A resource developed for female cancer survivors on nutrition and lifestyle to aid menopausal symptom management [Poster presentation].
- **Johnston, K. E.**, Cushen, S. J., Davis, A., Bermingham, K., Byrne, F., O'Grady, A., O'Neill, D., O'Connell, K., Raigal-Aran, L., Kearns, N., O'Reilly, S., Corrigan, M., Coulter, J., Collins, D., Cleary, V., Flavin, A., Murphy, A., Dahly, D. L., Palmer, B. A., Connolly, R. M., & Hegarty, J. (2023). LYSA (Linking You to Support and Advice) trial: The dietetic intervention component for a women's cancer survivorship pilot clinic [Poster presentation]. (Awarded the Dietetic Innovation Award)

Irish Nutrition and Dietetic Institute Research Symposium (2023)

- **Johnston, K. E**., Flynn, N. M., O'Connell, K., Ryan, A. M., & Cushen, S. J. (2023). Developing an evidence-based nutritional resource for symptom management in menopausal female cancer survivors [Poster presentation].

"Molecules to People" College of Medicine and Health, University College Cork (2022)

- **Johnston, K. E.,** Cushen, S. J., Davis, A., Bermingham, K., Byrne, F., O'Grady, A., O'Neill, D., O'Connell, K., Raigal-Aran, L., Kearns, N., O'Reilly, S., Corrigan, M., Coulter, J., Collins, D., Cleary, V., Flavin, A., Murphy, A., Dahly, D. L., Palmer, B. A., Connolly, R. M., & Hegarty, J. (2022). LYSA (Linking You to Support and Advice) trial: The dietetic intervention component for a women's cancer survivorship pilot clinic [Poster presentation].

Awards

Irish Nutrition and Dietetic Institute *Research Dietitian of the Year* 2026

Irish Cancer Society *PhD Researcher of the Year* 2026

Highly Commended at the Irish Nutrition and Dietetic Institute Research Symposium for *"*A dietitian-led medical oncology outpatient clinic for early-stage breast cancer survivors focused on weight gain concern and body composition: Results from the Linking You to Support and Advice "LYSA" randomised control trial." (2025)

Irish Cancer Society *Survivorship Project of the Year 2025*: "The Linking You to Support and Advice LYSA Trial"

Irish Association for Cancer Research 60th Satellite Survivorship Meeting *Best Social, Nursing and Allied Health Poster* (2024)

Irish Society of Clinical Nutrition and Metabolism and the Irish Nutrition and Dietetic Institute's *Dietetic Innovation Award* for the Dietetic Intervention Component of the LYSA Trial (2023)

Irish Cancer Society's *Social, Allied Health and Nursing Cancer Research Networking Award* for The Use of Novel Assessment Techniques to Assess Muscle Mass (2022 – 2024)

CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

Aspects of this work has been published in The Proceedings of Nutrition Society:

Keaver, L., O'Callaghan, N., Johnston, K. E., & Cushen, S. J. (2026). Nutrition in cancer survivorship: bridging the evidence-practice gap. Proceedings of the Nutrition Society, 1–12. doi:10.1017/S0029665125102152

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1.1 EARLY-STAGE BREAST AND GYNAECOLOGIC CANCER SURVIVORSHIP

1.1.1 Incidence of Breast and Gynaecologic Cancer

The International Agency for Research on Cancer (IARC), a World Health Organisation agency, projects that the incidence of new cancer cases from 2022 to 2045, excluding non-melanoma skin cancer, will increase by 61.3% worldwide in both sexes (1). In females, this projected trend is slightly lower at 55.5% (1). In 2022, 4.3% (n = 220,728) of the population in Ireland could be classed as a "cancer survivor" (2).

The Irish National Cancer Registry reported that 31.8% (n = 3,587) of invasive cancers diagnosed in 2020 to 2022 were breast; cervix uteri cancer made up 2.2% (n = 250) of all incidences and corpus uteri made up 5.1% (n = 571) (2). The National Cancer Registry also captures the numbers of persons diagnosed with cancer who were still alive at a particular point in time, reported as "complete prevalence". This includes those undergoing active treatment, and those engaged with palliative care. In 2022, breast cancer survivors accounted for 22% (n = 49,290) of those diagnosed with cancer; cervix uteri 2.3% (n = 5,047) and corpus uteri 2.9% (n = 6,362) (2).

Using the IARC *GLOBOCAN* database, in Ireland the projected incidence of breast cancer between 2022 to 2045 is expected to increase by 37.1%, a relatively large increase compared to the 8.1% Europe is projected to experience (3). Furthermore, cervical cancer is expected to rise by 15.3% in Ireland, compared to the 5.9% decline projected for Europe (3). Concerningly, endometrial cancer cases are expected to rise by 51.4%, a stark increase compared to the 9.1% increase projected for Europe (3). This growing population will require supportive care, services and resources to manage the late and long-term effects of cancer treatments, to support their long-term wellbeing and quality of life.

1.1.2 Treatment of Early-Stage Hormone Receptor Positive Breast and Gynaecologic Cancer

In Ireland, the European Society of Medical Oncology (ESMO) and the American Society of Clinical Oncology (ASCO) guidelines are used for the treatment of early-stage hormone-receptor positive breast and gynaecologic cancer. The treatment regimens are standardised by the National Cancer Control Programmes Systemic Anti-Cancer Guidelines.

As per the ESMO Early-Stage Breast Cancer Guideline, most early breast cancer cases can be cured by multimodality treatment. For most screening-detected, hormone-receptor positive, human epidermal growth factor negative breast cancer, surgery is the initial treatment modality (4). This can include a lumpectomy or a mastectomy.

The hormone receptor positive (HR+) subtype accounts for approximately 70% of breast cancers, and all are treated with an adjuvant endocrine therapy, regardless of stage. ESMO recommend the use of an adjuvant endocrine therapy for 5 years, increasing up to 7 to 10 years for higher stage cancers, reducing the risk of locoregional recurrence, distant metastatic recurrence and contralateral breast cancer, and improving overall survival (4). In HR+ cancers, active oestrogen receptor signalling drives tumour proliferation, and therefore oestrogen receptor antagonists (endocrine therapies) are used (5). Endocrine therapies are categorised according to their mechanism of action: aromatase inhibitors (anastrozole, letrozole, exemestane) and gonadotropin-releasing hormone agonists (goserelin) decrease endogenous oestrogen production whilst selective oestrogen receptor modulators (tamoxifen) directly antagonise oestrogen receptors (5).

The ESMO Clinical Practice Guideline reports that side effects of adjuvant endocrine therapy affect women of all ages and should be addressed to improve quality of life and adherence (4).

The ESMO Clinical Practice Guidelines for Cervical Cancer 2023 outline the range of treatment modalities, with an emphasis on fertility preservation (6). Treatments, such as pelvic exenteration (removal of organs including the bladder, urethra, rectum and anus), may lead to long-term side effects including permanent stomas.

1.2 IATROGENIC MENOPAUSE

The World Health Organisation and the International Menopause Society defines menopause as the permanent cessation of the menstrual cycle, resulting from the loss of ovarian follicular activity without any other pathological or physiological cause (7,8). The transition typically occurs in high-income countries between 45 and 55 years, with the average age of menopause occurring in Ireland at 51 years (7,8).

Early menopause occurs between the ages of 40 to 45 years and premature ovarian insufficiency occurs before the age of 40 years (9). A hormone receptor breast cancer, gynaecologic or haematologic cancer diagnosis and their subsequent treatments, including gonadotoxic chemotherapy, endocrine therapy, radiation and surgery, can lead to an early or induced (iatrogenic) menopause and/or menopausal symptoms (10–13) as summarised in Table 1.1.

There are a number of mechanisms that lead to early or iatrogenic menopause or premature ovarian insufficiency, and the joint burden of menopause and cancer impacts millions globally. Despite the significant clinical and global impact, accessible literature quantifying this burden remains limited, and there are still non consensus criteria for diagnosing menopause following cancer treatment (12).

Table 1.1 Mechanisms leading to menopause or menopausal symptoms in cancer patients modified from Szabo *et al*. (10)

Cancer Treatment	Indications For Treatment	How Does It Induce Menopause?
Chemotherapy Especially Cyclophosphamide, Procarbazine, and Other Alkylating Agents	Adjuvant therapy for premenopausal/perimenopausal breast cancer Chemotherapy for haematologic cancer Conditioning chemotherapy prior to stem cell transplant	Chemotherapy drugs can stop the ovaries from working properly, leading to treatment-induced menopause. This may be temporary or permanent depending on age, the type of drugs, the dose of drugs and the length of treatment. In some cases, it can lead to ovarian failure, causing chemotherapy-induced amenorrhea or premature menopause.
Radiotherapy Pelvic Radiation or Brachytherapy	Adjuvant and/or primary therapy for uterine, cervical vaginal, vulvar, bladder, anal, and colorectal cancers Pelvic Ewing sarcoma and infra-diaphragmatic nodal involvement in Hodgkin's lymphoma	Radiation to the pelvis as part of treatment for cervical cancer will lead to a premature menopause secondary to the ovaries receiving a small amount of radiation through radiation scatter. The ovaries are very sensitive to radiotherapy and therefore, this will result in a premature menopause. Noticeable hormonal changes will begin to occur three months after radiotherapy completion – however this varies case-by-case and could be sooner.
Anti-Oestrogen Endocrine Therapy	Adjuvant therapy for oestrogen-responsive breast cancers Risk-reducing medication for premenopausal women at high inherited risk of breast cancer (e.g. carriers of BRCA1 and BRCA2 genetic mutations)	Women who have been diagnosed with a hormone receptor positive breast cancer may be placed on an adjuvant hormone therapy. These may include tamoxifen or anastrozole and help reduce breast cancer recurrence and improve survival. Tamoxifen is known as a selective oestrogen receptor modulator (SERM). This means is blocks oestrogen in some cells, including on the breast, but not on others. Tamoxifen is used in both premenopausal and postmenopausal women. The treatment usually lasts between 5 – 10 years. Aromatase inhibitors, such as anastrozole, are used in women who are postmenopausal, and ovaries are no longer producing oestrogen. Aromatase inhibitors are used to block oestrogen production in other parts of your body. The treatment usually lasts between 5 – 7 years.

Surgery Removal of all Ovarian Tissue, Usually Bilateral Salpingo-Oophorectomy (With or Without Hysterectomy)	Diagnosis and/or treatment for ovarian and endometrial cancer Risk-reduction surgery for women at high risk of ovarian cancer (e.g. carriers of BRCA1 and BRCA2 genetic mutations)	For women diagnosed with cervical cancer, surgery often includes having both ovaries removed (bilateral oophorectomy) by itself or as part of a hysterectomy. As a result, menopausal status will change on the same day as surgery and symptoms will be prevalent. This is because the sudden loss of ovarian function. Often women who face surgically induced menopause experience symptoms that can be far more sudden, intense and traumatic. For women who have not had their ovaries removed as part of the hysterectomy, they will not experience menopausal symptoms as a result of their surgery.

There are a wide range of chemotherapy-induced amenorrhoea and premature ovarian insufficiency rates reported in the literature, from 15% up to 94% depending on definitions, age groups, regimens and follow-up (14). A narrative review indicated that high-risk chemotherapy regimens, such as cyclophosphamide combinations in older premenopausal women often yield >80% rates of ovarian failure, leading to iatrogenic menopause (15). Similarly Mar Fan et al. (2010) and Zhang et al. (2018) report on age-stratified outcomes, highlighting that young women have lower permanent-failure rates, and older premenopausal women, especially those over 40 years of age, have high rates (often >50%) of permanent menopause after standard chemotherapy (16,17). In objective biomarker evidence, a systematic review and meta-analysis reported that approximately 53% to 58% of breast cancer survivors over 40 years of age had very low Anti-Müllerin Hormone 12 to 24 months after chemotherapy (18).

Surgical and iatrogenic menopause and its symptoms may be more severe and of longer duration than that of a physiological menopause, and furthermore, a younger

age at menopause is associated with longer-term health risks, psychological and sexual dysfunction, and potentially cognitive dysfunction (19).

Those diagnosed with a hormone-sensitive cancer may pose a complex management challenge, due to the contraindication of hormone replacement therapy, limiting access to effective treatment, impairing quality of life and inducing psychological distress in some cases.

1.2.1 Symptoms

Symptoms of menopause result from hormonal fluctuations, primarily the decline in oestrogen levels. Up to 80%-90% of women will experience symptoms, with approximately 33% of those reporting that they were severe enough to impact their day to day quality of life (20). Symptoms can become more prominent at different time points around the menopause (21).

Menopausal status prior to cancer treatment and therapeutic agents used, such as chemotherapy and endocrine therapy, impact the specific symptoms and clinical challenges faced in iatrogenic menopause (22). In an aptly named systematic review "*It's not over when it's over…*", Harrington and colleagues (2010) highlighted that cancer survivors, including breast and gynaecologic, can experience symptoms for more than ten years following treatment, including cognitive limitations, depression and anxiety, fatigue, physical limitations, pain and sexual dysfunction (23). A 2024 systematic review and meta-analysis categorised 19 menopausal symptoms into four domains: somatic symptoms, psychological symptoms, urogenital symptoms and other symptoms (24) (Table 1.2). However, there are up to forty symptoms that have been identified in the literature and in Irish healthcare resources (Table 1.2).

Table 1.2: Categories of Menopausal Symptoms (*adapted from Fang et al 2024* (24) and Health Service Executive) .

Categories of Menopausal Symptoms Fang et al 2024 (24)**.**		**Categories of Menopausal Symptoms Health Service Executive (Cork and Kerry)**	
Domain	**Symptoms**	**Domain**	**Symptom**
Somatic	Hot flashes Sleep problems Heart discomfort Headaches Joint and muscular discomfort	Mood	Anxiety, irritability, low mood, tearfulness, mood swings, feeling overwhelmed, loss of confidence
Psychological	Physical and mental exhaustion Depression Anxiety Irritability Mood Swings	Cognitive	Reduced/lack of concentration, reduced focus and clarity of thought, reduced verbal fluency/problem with "word finding".
Urogenital	Sexual problems Vaginal dryness Urinary problems	Physical Symptoms	Palpitations, headaches, generalised aches and pains, joint stiffness, tinnitus, breast tenderness, dry eyes/nails, dry mouth, burning tongue/month, restless legs.
Other	Forgetfulness Difficult concentration Formication Change in the appearance, texture or tone of skin Increased facial hair Drying skin	Skin And Hair Symptoms	Dry hair, hair thinning, itchy skin, acne, increased facial hair, formication (feeling of insects crawling on skin).
		Gastrointestinal Symptoms	Bloating, constipation, irritable bowel syndrome symptoms.
		Hot Flushes	Hot flushes and night sweats.
		Genitourinary Symptoms	Vaginal dryness, vaginal itch, vaginal discharge, painful sex, overactive bladder, recurrent urinary tract infections, decreased arousal and orgasm, urinary incontinence, faecal incontinence, pelvic organ prolapse.
		Miscellaneous	Poor sleep, fatigue, low energy, low libido, dizziness.

Symptoms can impact the whole person, both physical and psychological, and often do not act in silos. The *Fang* et al (2024) Systematic Review and Meta Analysis reported prevalence of menopausal symptoms in 482,067 middle-aged women (24). The most prevalent symptom was joint and muscular discomfort (65.43%), followed by hot flashes (52.65%) (24). Joint and muscular discomfort is a notable symptom, particularly in those prescribed an adjuvant endocrine therapy, where arthralgias are a common side effect.

Cucciniello et al (2023) visualised endocrine therapy related toxicities that mirror those of a treatment-induced menopause (Figure 1.1). Unlike the aforementioned symptom lists, Cucciniello et al. (2023) include long-term chronic disease risks such as weight gain and dyslipidaemia (25).

It is acknowledged that many symptoms linked to iatrogenic menopause, resulting from anti-oestrogen endocrine therapy or surgery, may also arise from systemic anti-cancer treatments such as chemotherapy and radiotherapy. The following section differentiates between symptoms primarily associated with iatrogenic menopause and those more directly related to systemic anti-cancer therapies.

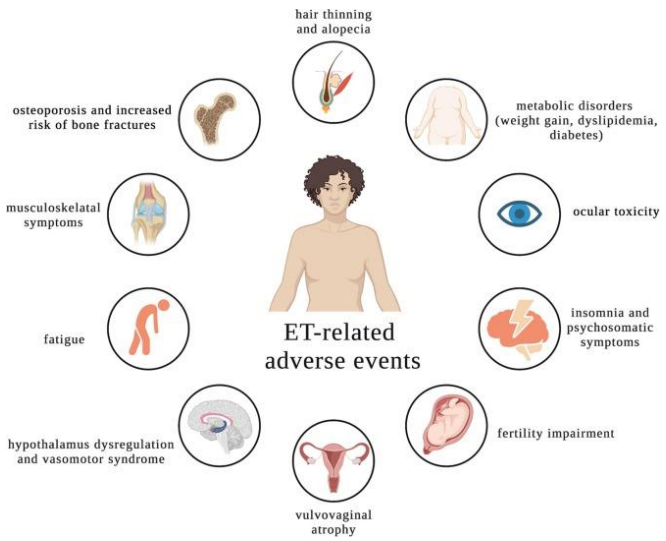


Figure 1.1: Endocrine-Therapy Related Adverse Events (Cuccinello et al., 2023) (25).

1.2.1.1 Vasomotor Symptoms: Hot Flushes and Night Sweats

Vasomotor symptoms, commonly known as hot flushes or night sweats, are the most frequent menopausal complaint. They result from declining oestrogen levels, which increase hypothalamic sensitivity to small changes in body temperature, triggering brief episodes of heat, sweating, palpitations, chills, or anxiety. Night sweats can disrupt sleep, negatively affecting cardiovascular, endocrine, and nervous system function and increasing the risk of hypertension, obesity, type 2 diabetes, and mood disorders. In women with oestrogen-receptor positive breast cancer, treatments such as gonadotoxic chemotherapy followed by ovarian suppression and oral endocrine therapy can produce more severe vasomotor symptoms than natural menopause (12,26,27). Aromatase inhibitors, recommended by ESMO guidelines for postmenopausal women (4), also induce or worsen hot flushes and night sweats (12,28). Vasomotor symptoms affect 65% of women after breast cancer treatment, particularly those on tamoxifen or aromatase inhibitors and those experiencing iatrogenic menopause (29–35).

An Australian study reported symptoms in 90% of breast cancer survivors six years post-diagnosis (36), while a 2023 review found over 95% of women on endocrine therapies are affected (25). On average, women report four to five hot flushes per day, though some experience up to twenty, with symptom duration ranging from six months to over 11 years (29,37,38). Predictors of vasomotor symptoms include chemotherapy (*adjusted odds ratio [aOR] 1.80, 95% CI 1.21 to 2.68*), adjuvant hormone therapy (*aOR 2.73, 95% CI 2.08 to 3.58*), and bilateral oophorectomy (*aOR 1.77, 95% CI 1.37 to 2.27*) (39). Bilateral salpingo-oophorectomy without concurrent

hormone replacement therapy is associated with more frequent and severe symptoms (29,40–42).

Given their high prevalence, prolonged duration, and potential exacerbation by cancer treatments, vasomotor symptoms represent a substantial burden on quality of life, highlighting the need for proactive recognition and management in both natural and iatrogenic menopause.

1.2.1.2 Gastrointestinal and Genitourinary Symptoms

1.2.1.2.1 Symptoms Attributable to Systemic Anti-Cancer Treatments

Gastrointestinal symptoms, referring to symptoms of the mouth oesophagus, stomach, small and large intestine, rectum and anus, are the most common of all cancer treatment side-effects and have the greatest impact quality of life and day-to-day activities (43). Muls (2013) has identified twenty-three lower gastrointestinal symptoms as a result of cancer treatments, including bleeding, bloating, changes in bowel habits, constipation, diarrhoea, incontinence, nausea, steatorrhea, urgency, nausea, vomiting and weight loss (43). These symptoms can severely impact an individual's quality of life and day-to-day activities (44).

Common chemotherapy agents used in breast cancer treatment including methotrexate and 5-fluorouracil are likely to cause diarrhoea, whereas chemotherapy agents used in the treatment of gynaecologic cancers, such as cisplatin and carboplatin (platinum agents) are likely to cause constipation (43). In gynaecologic cancers, external and internal (brachytherapy) beam radiotherapy to the ovaries or cervix acutely damage the gut due to the surrounding normal tissues being exposed to radiation (45). The extent of damage is influenced by radiation dosage, treatment duration, area of bowel involved, and concurrent chemotherapy (46). A further consideration must be given to

patients undergoing radiation with concurrent chemotherapy, as chemotherapy can increase the sensitivity of non-cancerous tissue to radiation damage, and therefore may increase symptomology (46).

Symptoms of radiation-induced gastrointestinal damage typically begin around two weeks after treatment initiation and may resolve within three to nine months (43). While most patients' gastrointestinal symptoms resolve over time, 10% to 20% may develop persistent or delayed toxicities over a ten-year follow-up, underscoring their long-term burden. Fernandes and Andreyev (2021) note that more individuals develop pelvic radiation disease each year than are diagnosed with irritable bowel disease (45), highlighting its importance as a clinical and research priority.

1.2.1.2.2 Symptoms Attributable to Iatrogenic Menopause

In addition to chemotherapy and radiotherapy, iatrogenic menopause can contribute to gastrointestinal and genitourinary symptoms. Declining oestrogen and progesterone levels affect neurons in the myenteric plexus, slowing gut motility and causing constipation and abdominal discomfort (47,48). This may exacerbate symptom clusters observed in midlife women, with 46% experiencing mild, 44% moderate, and 10% severe gastrointestinal symptoms during menopause (49).

Similarly, abrupt or treatment-induced menopause can trigger genitourinary syndrome of menopause, a chronic condition affecting the vulvovaginal, sexual, and lower urinary tract due to declining oestrogen (50–52). Symptoms include urinary frequency, incontinence, vaginal dryness and itching, decreased libido, dyspareunia, and recurrent urinary tract infections, and are associated with more severe sexual dysfunction and reduced quality of life compared to physiological menopause (51) (Table 1.3).

Female genitalia and lower urinary tracts rely on oestrogen to maintain normal physiology, including vaginal lubrication, epithelial proliferation, and tissue elasticity (50,51,53). During menopause, declining oestrogen reduces receptor density, collagen, elastin, hyaluronic acid, and blood flow, causing vaginal thinning, muscle weakening, tissue stiffening, and symptoms such as dryness, discomfort, and irritation (51,54,55). Genitourinary syndrome of menopause is particularly prevalent in younger patients receiving endocrine therapy or chemotherapy and affects 50% to 90% of women with breast or gynaecologic cancer (56–60). Overall, it is a common, multifactorial consequence of both natural and treatment-induced menopause, with important implications for survivorship care.

Table 1.3: External Manifestations of Genitourinary Syndrome of Menopause (adapted from Gandhi et al., 2016) (51)

Genital Signs and Symptoms	Urological Signs and Symptoms	Sexual Signs and Symptoms
Vaginal / pelvic pressure and pain	Frequency of urination	Loss of libido
Dryness	Urgency of urination	Loss of arousal
Irritation / burning	Postvoid dribbling	Lack of lubrication
Decreased elasticity	Nocturia	Dyspareunia (pain during sexual intercourse)
Suprapubic pain	Stress or urgency incontinence	Pelvic pain
Labial shrinking	Dysuria (sensation of pain, burning, stinging or itching during urination)	Bleeding or spotting during sexual intercourse
Increased vaginal friability	Haematuria	
	Recurrent urinary tract infections	

1.2.1.3 Psychological Symptoms: Cognition and Fatigue

Psychological symptoms during menopause, including low mood, anxiety, cognitive difficulties, irritability, and fatigue, affect approximately two-thirds of women and can substantially impact quality of life (61). Declining oestrogen contributes to these symptoms via neuroprotective and neurotrophic effects, modulation of neurotransmitters such as dopamine and serotonin, and regulation of central glucose metabolism, aerobic glycolysis, and mitochondrial function, particularly in brain regions integral to memory and executive function (62–66). Surgical or treatment-induced menopause accelerates cognitive decline, with studies reporting deficits in verbal and semantic memory, processing speed, and executive function (all $p < 0.05$) (67,68).

Cancer treatments further exacerbate these effects. Cognitive impairment is observed in 13% to 70% of breast cancer patients and survivors, with endocrine therapy linked to poorer performance on neuropsychological tests compared to non-cancer controls (23,68–71). Fatigue is reported in 60% of women on endocrine therapies (25), with aromatase inhibitors and combination chemotherapy-endocrine treatments associated with moderate to severe fatigue, increased anxiety, and reduced quality of life (72–75). Cancer-related uncertainty, particularly in younger survivors, further contributes to fatigue and psychological distress (76).

Collectively, these findings underscore the complex interplay between menopausal status, oestrogen depletion, and cancer treatments in shaping psychological wellbeing, cognitive function, and fatigue, with significant implications for quality of life in affected women.

1.2.1.4 Body Composition Alterations: Muscle Mass and Bone Health

1.2.1.4.1 Alterations Attributable to Iatrogenic Menopause

Declining oestradiol during iatrogenic menopause impacts musculoskeletal tissue, including bone, muscle, cartilage, ligaments, and adipose tissue, contributing to the musculoskeletal syndrome of menopause, which encompasses inflammation, sarcopenia, osteoporosis, and arthritis (77). Signs of inflammation, such as arthralgia and joint discomfort, increase across the menopausal transition, peaking in early post menopause.

Oestrogen deficiency accelerates bone loss, as it normally regulates bone resorption and formation (78). In cancer patients, this is pronounced: within six months of treatment, bone density can decrease by 21% compared to age-matched menstruating women (79,80). Postmenopausal breast cancer survivors prescribed aromatase inhibitors and GnRH agonists experience an annual bone loss rate 7.7% higher than the general population (81). Osteoporosis increases fracture risk and is associated with loss of height, back pain, and stooped posture.

Sarcopenia, declines in skeletal muscle mass, strength, and function, is also exacerbated by oestrogen deficiency (77,82). Its prevalence rises with age, and it is associated with impaired physical performance, mobility limitations, falls, reduced ability in daily activities, hospitalisation, poorer quality of life, and higher mortality (83). Sarcopenia may be primary (age-related) or secondary (due to nutrition, activity, or disease, including cancer) (84).

Women undergoing endocrine therapy with low muscle mass are more likely to discontinue treatment due to toxicity (*OR 2.18*, $p = 0.036$), which is linked to worse ipsilateral breast tumour recurrence (*HR 9.47*, $p = 0.002$) and reduced disease-free

survival (*HR 4.53*, *p = 0.001*) (85). A 2024 systematic review reported a 38% prevalence of sarcopenia in breast cancer patients (*95% CI: 29% to 48%)* and found it increased mortality risk (*HR 1.77, 95% CI 1.35 to 2.32*, *p ≤ 0.001*) (86). However, interpretation of these findings warrants consideration of the heterogeneous diagnostic criteria used across oncology studies. Although classified as sarcopenia, many studies relied primarily on imaging-derived measures of muscle mass, often without concurrent assessment of muscle strength or physical performance as recommended by contemporary consensus definitions. Consequently, some reported estimates may more accurately reflect the prevalence and prognostic significance of low muscle mass rather than clinically confirmed sarcopenia.

1.2.1.4.2 Alterations Attributable to Systemic Anti-Cancer Treatment

Sarcopenia is increasingly recognised as an important concern in gynaecologic cancers because of its association with adverse clinical outcomes. However, much of the oncology literature has focused on low muscle mass rather than clinically confirmed sarcopenia. Low muscle mass, commonly identified using skeletal muscle index cut-points derived from cross-sectional imaging, affects approximately 30.1% of cervical cancer patients and 25.8% of endometrial cancer patients (84). A ≥7% decline in skeletal muscle index during treatment predicts poorer prognosis, with significant reductions in progression-free and overall survival (84). A systematic review and meta-analysis across gynaecologic malignancies (n = 2,446) reported sarcopenia was associated with lower progression-free survival (*HR 1.69, 95% CI 1.03 to 2.76*) and overall survival (*HR 1.33, 95% CI 1.08 to 1.64*), with adjusted hazard ratios remaining significant despite potential publication bias (87). However, the included studies used heterogeneous definitions, with many relying on imaging-derived measures of muscle mass rather than comprehensive assessments

incorporating muscle strength and physical performance. Therefore, these findings may partly reflect the prognostic significance of low muscle mass rather than clinically confirmed sarcopenia according to contemporary diagnostic criteria. Despite its prognostic importance, muscle mass assessment is often underemphasised in outpatient survivorship care, with clinicians prioritising immediate concerns such as disease recurrence and treatment side effects.

1.2.1.4.3 Sarcopenic Obesity

Sarcopenic obesity, defined as the coexistence of excess adiposity and impaired muscle function with low muscle mass, is recognised as a distinct clinical condition by The European Society of Clinical Nutrition and Metabolism (ESPEN) and the European Association for the Study of Obesity (EASO) (88). Assessment involves a two-step process: first, evaluation of skeletal muscle function (e.g., handgrip strength, sit-to-stand test), and second, body composition analysis using appendicular lean mass by dual-energy x-ray absorptiometry (DEXA) or total skeletal muscle mass by bioelectrical impedance analysis (BIA), with both altered function and composition required for diagnosis. Screening requires elevated BMI or waist circumference plus surrogate indicators of sarcopenia (88). Staging defines Stage I as sarcopenic obesity without complications and Stage II as the presence of at least one complication, such as metabolic, cardiovascular, respiratory, or functional disability (88). Sarcopenic obesity is independently associated with higher mortality and increased systemic and surgical treatment complications across multiple cancer types (89).

While sarcopenic obesity is formally defined by the coexistence of excess adiposity and impaired muscle function with reduced muscle mass, many oncology studies

have relied solely on imaging-derived measures of muscle quantity without assessment of muscle strength or physical performance. Consequently, some reported associations between “sarcopenic obesity” and adverse cancer outcomes may more accurately reflect the prognostic impact of low muscle mass in the presence of obesity rather than clinically confirmed sarcopenic obesity according to current ESPEN and EASO criteria. This distinction is important when interpreting the oncology literature and highlights the need for comprehensive assessment approaches that include both body composition and functional measures.

1.2.1.5 Body Composition Alterations: Adipose Tissue Mass and Weight Gain Concern

Obesity is a significant risk factor for postmenopausal breast and endometrial cancer and is common among survivors. Up to 90% of breast cancer patients experience weight gain after treatment, which may influence disease-free survival (90–92). Hormonal changes, including declining oestrogen, contribute to increased total and abdominal fat, though adjuvant endocrine therapy shows inconsistent associations with weight gain, with prevalence over five years ranging from 18% to 55% (93,94). Recent data report that 52% of survivors on endocrine therapy gained a clinically significant mean of 3.5 kg in premenopausal and 0.6 kg in postmenopausal women over five years (90).

Although weight gain is commonly reported following cancer treatment, body weight and BMI alone may not adequately capture clinically important changes in body composition. Survivors may simultaneously experience increases in adiposity and reductions in skeletal muscle mass despite relatively stable body weight, a phenomenon that may be obscured when relying solely on BMI-based assessment. Emerging evidence suggests that visceral adiposity, intramuscular fat infiltration,

and low muscle mass may be more strongly associated with treatment toxicity, physical function, cardiovascular risk, and survival outcomes than body weight alone. Consequently, assessment of body composition may provide a more clinically meaningful evaluation of nutritional and metabolic health among cancer survivors than weight-centred measures alone.

Obesity increases mortality and recurrence risk in breast cancer. Pre-diagnosis obesity raises total mortality by 17% per 5 kg/m² and breast cancer–specific mortality by 18% (95), while ≥10% post-diagnosis weight gain is associated with 23% higher mortality (96). Meta-analysis of 46 studies found obesity linked to 34% increased all-cause mortality (*HR 1.34, 95% CI 1.12 to 1.59*) and 28% increased recurrence risk (*HR 1.28, 95% CI 1.06 to 1.56*) (97). Mechanistically, excess adipose tissue acts as an endocrine organ, increasing oestrogen production; postmenopausal women with BMI >30 kg/m² had 35% higher oestrone and 130% higher oestradiol compared to BMI <22 kg/m², promoting tumour growth and poorer outcomes (98,99).

Obesity also contributes to metabolic syndrome, encompassing abdominal obesity, hypertension, hyperglycaemia, dyslipidaemia, and increased cardiovascular risk (100). In breast cancer survivors, higher visceral and intramuscular adiposity increases cardiovascular disease risk (*HR 1.15, 95% CI 1.03 to 1.29; HR 1.21, 95% CI 1.06 to 1.37*) even in individuals with healthy BMI (101).

Collectively, these findings reinforce the dual burden of obesity in breast cancer survivors, influencing both oncologic outcomes and cardiovascular disease risk, thereby necessitating integrated approaches to long-term management.

1.2.1.6 Cardiovascular Disease Risk

Cardiovascular disease (CVD) is the leading cause of death in women, surpassing all cancers combined (102). Menopause contributes to cardiometabolic changes, including shifts in body fat distribution, lipoprotein alterations, and endothelial fluctuations (102,103). Breast cancer survivors face additional latent cardiac effects from treatment, including endocrine therapy, chemotherapy, and radiotherapy, ranging from hypertension to heart failure, with the highest CVD risk emerging around seven years post-diagnosis (104). In older survivors, the development of CVD risk factors often exceeds the risk of cancer recurrence (104).

1.2.1.6.1 Cardiovascular Risk Attributable to Iatrogenic Menopause

Breast cancer survivors face increased cardiovascular risk. A meta-analysis found they were more likely to die from cardiovascular disease than matched non-cancer populations in the first five years post-diagnosis (*HR 1.09, 95% CI 1.07 to 1.11*) (105). A broader 2025 meta-analysis of 160 studies (n = 49,395,865) reported that cancer survivors overall had a 47% higher risk of cardiovascular disease (*HR 1.47, 95% CI 1.33 to 1.62*), with consistent elevation seen in breast, brain, haematologic, respiratory, and male genital cancer survivors (106).

Endocrine therapies further influence cardiovascular risk. Tamoxifen increases venous thromboembolism risk, whereas aromatase inhibitors are linked to higher risks of myocardial infarction and ischemic stroke (*OR 1.30, 95% CI 0.88 to1.93; OR 1.39, 95% CI 1.07 to 1.81*), along with adverse lipid changes, though venous thromboembolism is less frequent with aromatase inhibitors (*OR 0.61, 95% CI 0.37 to 1.00*) (107,108).

Premature and early menopause are also associated with increased cardiovascular risk. A 2023 meta-analysis (nine cohorts, n = 6,255,783) found premature and early

menopause elevated risks of heart failure (*HR 1.39, 95% CI 1.31 to 1.47; HR 1.23, 95% CI 1.10 to 1.37*) and atrial fibrillation (*HR 1.15, 95% CI 1.01 to 1.31; HR 1.08, 95% CI 1.04 to 1.13*), with the strongest associations seen in premature menopause (109).

1.2.1.6.2 Cardiovascular Risk Attributable to Systemic Anti-Cancer Treatments

Gernaat et al. (2017) highlighted that breast cancer survivors may find themselves at risk of cardiovascular disease due to the combination of high cancer incidence, improved survival, presence of cardiovascular disease risk factors and cardiotoxic breast cancer treatments (110). Overall, the elevated cardiovascular risk in breast cancer survivors appears multifactorial, reflecting both treatment-related cardiotoxicity and the exacerbation of pre-existing cardiometabolic changes, and pointing to an urgent need for further research to guide prevention and long-term management strategies.

1.2.2 Menopausal Symptoms and Adherence to Systemic Anti-Cancer Treatments

In hormone receptor-positive breast cancer survivors, menopausal symptoms are a major barrier to adherence to adjuvant endocrine therapy, particularly given limited options such as hormone replacement therapy. Despite endocrine therapy's proven role in reducing recurrence and improving survival, non-adherence affects 25% to 55% of women, with adverse effects, especially oestrogen withdrawal symptoms, being the primary driver (29,111,112). Early discontinuation is associated with a 26% increase in all-cause mortality (111,113).

Observational studies highlight the scale of the problem. In a US survey (n = 373), 81% reported side effects, with 12% discontinuing therapy; discontinuation rates

were fourfold higher among those on extended therapy beyond five years (114). In New Zealand (n = 1,213), adherence fell from 90% in year one to 50% by year five, with 20% stopping due to poor tolerability (115). Systematic reviews report adherence declines of ~25% over five years, influenced by adverse effects, patient beliefs, and healthcare system factors influences (116,117).

Patient-reported outcomes reinforce the central role of symptoms. Integrative and qualitative reviews identify musculoskeletal pain, cognitive and gynaecologic symptoms, weight gain, gastrointestinal complaints, and menopausal symptoms as key contributors to non-adherence, particularly during the first six months (118,119). Women often describe a "horned dilemma," balancing severe side effects against fear of recurrence (120,121). Healthcare professionals report challenges managing expectations and supporting patients, with limited allied health involvement and gaps in non-pharmacological interventions (122,123).

Collectively, these findings highlight that unmanaged treatment-related symptoms remain the dominant barrier to adherence, underscoring the need for effective supportive strategies to prevent avoidable discontinuation and the risk of disease recurrence.

1.2.3 Pharmacologic vs Non-Pharmacologic Treatments

Managing menopause after cancer can be complex, particularly for those with hormone-sensitive diagnoses. Hormone replacement therapy, following results from the prematurely stopped HABITS (Hormonal replacement therapy After Breast cancer – Is iT Safe?) Trial and the Stockholm Trial (134), is contraindicated in breast cancer due to the increased risk of recurring breast cancer events.

The NICE (National Institute for Health and Care Excellence) Guideline (NG23) "Menopause: Identification and Management" advises caution for HRT use in women with a personal history or high inherited risk of breast cancer, highlighting the use of alternative non-hormonal treatments, such as cognitive behavioural therapy, to manage menopausal symptoms (125).

In the first paper of *The Lancet's* 2024 Menopause Series, authors highlighted a new approach, encompassing an empowerment model that surpasses symptom specific treatment, putting the patient as an equal and active partner in managing their own care (126). The review noted that future research point towards identifying personalised treatments for those with specific symptoms or those identified by digital health measures (136). Furthermore, Hickey and colleagues (2024) called for the needs of skilled clinicians with the ability to provide evidence-based strategies to relieve menopausal symptoms (126).

In the Irish context, Donohoe et al. (2023) summarised the available data surrounding the treatment of menopausal symptoms following a cancer diagnosis (22). Whilst there was definitive data for pharmacological options, authors highlighted that whilst up to 50% of women use non-pharmacologic therapies to manage menopausal symptoms, many of these are not supported by high quality evidence (11,127). Non-pharmacologic treatments for menopausal symptom management include talking therapies, hypnosis, yoga and acupuncture. However, their evidence is limited (12). In the early 2000s-2010s it was reported that complementary therapies, including the use of herbal therapies, are used by 40% to 50% in Western countries to manage menopausal symptoms (128–130). In 2013, 55.7% (n = 226) of Irish breast cancer survivors surveyed reported the use of complementary alternative medicine, 32.8%

used dietary interventions, including herbal medications and health supplements, to reduce symptoms and side effects of treatment (128).

1.3 NUTRITIONAL CONSIDERATIONS IN EARLY-STAGE BREAST AND GYNAECOLOGIC CANCER SURVIVORSHIP

The following sub-chapter addresses the nutritional considerations of the aforementioned symptoms and late-effects attributable to systemic anti-cancer treatments and iatrogenic menopause.

1.3.1 Current Dietary Guidelines

There are limited comprehensive dietary guidelines for cancer survivors, particularly for breast and gynaecologic cancer survivors, that fully encompass the unique nutritional needs of this population.

The European Society of Clinical Nutrition and Metabolism (ESPEN) published guidelines in 2017 and a practical guideline in 2021 which briefly outlines the two recommendations made for "cancer survivors" (131,132). The first lifestyle recommendation is that cancer survivors engage in regular physical activity (strong strength of recommendation, low level of evidence) (132). The second lifestyle recommendation highlights that cancer survivors should maintain a healthy weight (BMI 18.5kg/m^2 – 25kg/m^2) and maintain a healthy lifestyle, including being physically active, and a diet based on vegetables, fruits and whole-grains, and low in saturated fat, red meat and alcohol (132). The second recommendation has a strong strength, and low level of evidence (strong consensus) (132). Furthermore, the commentary behind the recommendation states that survivors with overweight or

obesity should strive to reduce weight and preferably until a healthy BMI has been reached (132). Interestingly, there were no tumour-specific recommendations made.

In contrast, the American Cancer Society (ACS) published a comprehensive guideline on physical activity and nutrition for cancer survivors in 2022 (133). Whilst the guideline does not provide any explicit recommendations around dietary intake, it does provide a high-level overview of available guidelines and research regarding tumour-specific recommendations (133). Notably, the ACS guideline highlights that survivors' nutritional intake can be negatively impacted by symptoms relate to the tumour or treatment, and that this should be identified and managed (133). The guideline summarises that in breast cancer survivors greater obesity is associated with higher risk of recurrence, tumour-specific and overall mortality; physical activity is associated with reduced risk of tumour-specific and all-cause mortality; more "healthful" dietary patterns are associated with lower risk of overall and non-breast cancer morality; and food-based soy consumption before diagnosis is associated with lower risk of overall mortality (133). The guideline also highlights that existing evidence surrounding alcohol intake and breast cancer recurrence and mortality is limited and inconsistent overall, with more research warranted for oestrogen receptor positive sub-types and menopausal status (133). In relation to gynaecologic cancers, there is limited and inconclusive evidence to make recommendations relating to diet and cancer, warranting further studies to make concrete recommendations (133).

The NCCN Survivorship Guidelines recommend that a multi-disciplinary approach is used and that providers should be competent advising survivors how to achieve an optimal body composition, including low overall body fat and higher amounts of

muscle mass (134). In a 2025 Guideline Insight, Sanft et al. (2025) recommend that survivors should follow a predominantly nutrient rich, plant-based diet and make informed choices about food, promoting variety and adequate nutritional intake (135). The guideline highlights recommended sources of dietary components, including fat (plant sources such as olive oil, canola oil, avocado, seeds and nuts and cold water fish); carbohydrates (fruit, vegetables, wholegrains and legumes); and protein (poultry, fish, legumes, low-fat dairy foods, eggs and nuts) (135). Furthermore, the guideline reports that consumption of red meat, processed meats, processed foods high in fat, starches or sugars and refined sugars should be limited (135).

Furthermore, the NCCN Survivorship Guideline Insights (v2 2025) outline specific recommendations for survivors with healthy weight, underweight or overweight/obesity as per the World Health Organisation BMI classifications (136). Similar to the ESPEN Clinical Nutrition in Cancer guidelines, Sanft et al. (2025) highlight that maintaining a healthy BMI of between 18.5kg/m^2 – 24.9kg/m^2 should be encouraged; intentional weight loss and weight gain should be a priority for survivors who have overweight or obesity and underweight respectively (135). Notably, the guideline highlights that survivors should be assessed for metabolic health and body composition, independent of their BMI (135).

The European Society of Medical Oncology (ESMO) and the American Society of Clinical Oncology (ASCO) both briefly mention lifestyle factors or nutritional considerations in their Early Breast Cancer guidelines (4,137). The ESMO guidelines recommend that patients with early breast cancer should be encouraged to adopt a healthy lifestyle, avoid being overweight, exercise regularly and minimise alcohol intake (4). The ASCO guidelines do not explicitly recommend any nutritional

considerations. However, they recommend starting bone density monitoring or the initiation of bone-modifying therapy to reduce the incidence of osteoporosis among aromatase inhibitor therapy recipients (137).

The Clinical Oncology Society of Australia's position statement on survivorship care emphasises the need for supporting wellness, healthy lifestyle and primary and secondary cancer prevention with referral to allied health professionals and evidence-based programmes (138). Furthermore, the position statement prioritises the role of lifestyle behaviour change programmes in long-term prevention, minimisation and management of symptoms and late effects of cancer and its treatment (138), aligning with NCCN Survivorship Guidelines.

Following the completion of curative systematic anti-cancer treatment many survivors are recommended to follow general healthy eating advice. In Ireland, this healthy eating advice is conveyed by the Healthy Ireland Food Pyramid (139). The visual guide was developed and launched in 2016 as part of the Healthy Ireland's Healthy Food for Life campaign commissioned by the Department of Health (139).

Looking towards the needs of cancer survivors who have experienced an iatrogenic menopause, in 2020 the European Society of Menopause and Andropause (EMAS) released a position statement on the Mediterranean diet and menopausal health (140). The Society endorsed the use of this style of eating, reporting that long-term adherence may improve bone mineral density; prevent cognitive decline; improve cardiovascular risk, events and death; and reduce the risk of breast cancer and all-cause mortality (140).

Despite the growing recognition of the importance of lifestyle and nutrition in survivorship, current dietary guidelines for cancer survivors remain generic, fragmented, and lacking in specificity for high-need groups such as women with hormone receptor-positive breast cancer, gynaecologic cancers, or those experiencing iatrogenic menopause. While ESPEN and ESMO provide only broad recommendations around healthy weight, physical activity, and plant-based diets, based on low-level evidence and without tumour-specific nuance, the ACS guideline goes further by linking obesity, diet, and physical activity with outcomes in breast cancer, yet still falls short of offering concrete, individualised dietary strategies. NCCN survivorship guidelines incorporate a multidisciplinary perspective and body composition assessment but again focus on broad "healthy eating" principles rather than addressing the unique metabolic and endocrine challenges faced by these populations. The Clinical Oncology Society of Australia model of care emphasises a more holistic approach to survivorship involving allied health professionals with a focus on symptom management and long-term health. General population dietary frameworks, such as Ireland's Food Pyramid, provide useful visual tools but are not designed with cancer survivorship in mind. The EMAS Position Statement, whilst a significant improvement in dietary recommendations for individuals experiencing menopause and its symptoms, is also not designed with cancer survivorship in mind. Overall, the absence of detailed, evidence-based, and cancer-specific nutritional recommendations, particularly for HR-positive breast cancer, gynaecologic cancers, and iatrogenic menopause, represents a critical gap in survivorship care.

1.3.2 Muscle Mass

Muscle mass is an important prognostic factor in cancer that has been well documented in the literature (141). However, it is not routinely assessed in hormone receptor positive breast cancer survivors due to a myriad of factors. A lack of standardised protocols, limited access to specialised equipment such as bioelectrical impedance analysis or DEXA scans, and limited trained personnel are all barriers to muscle mass assessment in outpatient clinics (142). Whilst assessing muscle mass may not be seen as a high priority in outpatient clinics, muscle mass is directly related to adjuvant endocrine therapy outcome (85). Oncology dietitians, who have upskilled in body composition, are in the unique position to assess, prevent and manage those at risk of low muscle mass, and sarcopenia, (the accelerated loss of skeletal muscle mass and function commonly, but not exclusively, associated with advancing age) (143). Personalised nutritional counselling is vital to managing low muscle mass and sarcopenia risk, by ensuring optimal protein intake throughout the day.

For individuals with a cancer diagnosis, protein intake recommendations generally exceed those of the general population to support maintenance of lean body mass and counteract treatment-related catabolism. The European Society for Clinical Nutrition and Metabolism (ESPEN) guideline recommends a protein intake of at least 1.0 g/kg body weight/day, with intakes up to 1.5 g/kg body weight/day suggested where feasible to support nutritional status and preserve lean tissue (131,132). Higher intakes (up to approximately 2.0 g/kg body weight/day) have also been proposed in the literature to support positive protein balance in specific physiological or clinical contexts; however, this represents an upper theoretical target rather than a formal guideline recommendation (144).

Protein intake in the Irish population is generally lower than these recommended levels and declines with increasing age, with intake also unevenly distributed across the day (145,146). This may contribute to vulnerability to loss of muscle mass, particularly in women undergoing iatrogenic menopause, where hormonal changes further exacerbate age- and disease-related declines in skeletal muscle. Cancer additionally disrupts normal muscle protein turnover, thereby increasing protein requirements. Amino acid availability and dietary protein quality also influence muscle protein synthesis, with evidence suggesting that higher-quality protein sources, particularly animal-based proteins or mixed dietary patterns incorporating both animal and plant sources, may provide a greater anabolic stimulus for muscle maintenance (144).

Despite these recommendations, there is limited explicit guidance for long-term cancer survivors, particularly those affected by ongoing metabolic and musculoskeletal consequences of systemic anti-cancer therapies and endocrine treatment. In this context, Saraf et al. (2024) reported that low muscle mass is associated with increased risk of toxicity-related discontinuation of adjuvant endocrine therapy (OR 2.18, $p = 0.036$) (85), highlighting the importance of optimising nutritional intake to support muscle maintenance in breast cancer survivorship.

Without clear guidance on protein intake in survivorship, the clinical relevance of muscle mass loss becomes increasingly important, yet it remains insufficiently addressed in routine oncology practice. Assessment of muscle mass is not consistently incorporated into medical oncology outpatient care, despite being recognised as a common and clinically relevant nutritional issue with implications for prognosis in oncology populations (141). In a 2023 cross-sectional survey of Irish dietitians,

although 98.8% agreed that muscle mass is an important component of nutritional assessment, the frequency of formal assessment in clinical practice remained low (148).

A range of techniques are available for the assessment of muscle mass. Computed tomography (CT) is often considered a reference method in research settings due to its accuracy and ability to quantify skeletal muscle at specific anatomical landmarks; however, its clinical use is limited by cost, lack of accessibility, and exposure to ionising radiation. Magnetic resonance imaging (MRI) provides similar accuracy without radiation exposure but is limited by cost and availability in routine practice. Dual-energy X-ray absorptiometry (DXA) is more widely available and provides estimates of lean mass, but does not directly measure skeletal muscle and may be influenced by hydration status. Bioelectrical impedance analysis (BIA) offers a low-cost, portable, and non-invasive alternative suitable for outpatient and survivorship settings, although its accuracy may be affected by hydration status and there is variability in population-specific cut-off values (142). Ultrasound has emerged as a promising bedside technique for assessing muscle thickness and quality, although it is operator-dependent and currently lacks standardised protocols in oncology populations (142,149). Anthropometric measures such as mid-upper arm circumference are also used in clinical settings but have limited sensitivity for detecting early changes in muscle mass.

Despite increasing availability of these techniques, implementation in clinical practice remains limited. In the Irish context, a survey of dietetic practice found that handgrip strength was the most commonly used marker of muscle function (64.3%), whereas

more direct body composition methods such as CT and BIA were used infrequently (1.4% and 14.2%, respectively) (148). This highlights a clear gap between awareness of the importance of muscle assessment and its routine application in clinical practice.

While BIA and other accessible methods offer practical solutions for outpatient and survivorship care, there remains limited consensus regarding diagnostic cut-off values for low muscle mass and sarcopenia when using these techniques. Reported thresholds for skeletal muscle index vary considerably across studies, ranging from approximately 5.45 kg/m² to 6.75 kg/m² depending on population and methodology (Table 1.4). Aleixo et al. have suggested that BIA can provide valid estimates of body composition in cancer populations, particularly in pre-treatment settings (150).

Table 1.4: A Brief Review of the Literature Including Adapted Results from Aleixo et al. Systematic Review of Bioelectrical Impedance Analysis Derived Sarcopenia Definitions (150)

Authors	Year	Country	n	Modality	Age (years) Mean [SD]	Tumour Location	Inclusion/Exclusion Criteria of note	Stage of Care	Female Specific Sarcopenia Definition	Sarcopenic (%)	Sarcopenic Obese (%)
Prado et al. (151)	2018	Canada	2,276	Valhalla 1990B	71 [8]	NHANES III			SMI <6.76kg/m2		
Otten et al. (152)	2017	Germany	439	Nutriguard M	69.6 [6.2]	Multiple	>60 years, consecutive solid or hematologic tumour disease of any type or stage	Pre chemotherapy or radiation or surgery, or no treatment	SMI <6.75kg/m2	27.1	NR
Oflazgolu et al. (153)	2019	Turkey	461	TANITA SC 330	58.2 [11.1]	Multiple	>18 years, newly diagnosed early stage or metastatic cancer	Pre chemotherapy or radiation or surgery	SMI <6.75kg/m2	16.7	NR
Wang et al. (154)	2024	China	150	InBody 770	57.1 [11.7]	Lung, Cervical	>18 years, newly diagnosed lung or cervical cancer scheduled for systemic anti-cancer treatment	Scheduled Treatment	ASMI <5.7kg/m² *(indicated low muscle mass)*	22	NR

Abbreviations: ASMI, Appendicular Skeletal Muscle Index; NR, Not Reported; SMI, Skeletal Muscle Index.

However, other evidence indicates variability in diagnostic performance depending on clinical context, with reduced precision in outpatient survivorship populations and inconsistency in cut-off standardisation (142). Nevertheless, BIA is considered feasible for routine monitoring due to its practicality, cost-effectiveness, and repeatability in clinical settings.

Muscle mass is therefore a clinically relevant prognostic factor in breast and gynaecologic cancer survivorship, influencing treatment tolerance and long-term outcomes, yet it is not routinely assessed in outpatient oncology care due to limitations in standardisation, access, and clinical integration. Improving the implementation of feasible and standardised muscle assessment tools, alongside appropriate nutritional strategies including adequate protein intake, may support earlier identification of low muscle mass and enable more proactive dietary intervention. This is particularly relevant in survivorship populations where individuals may appear clinically well despite underlying changes in body composition. Integrating feasible assessment approaches into routine dietetic care may therefore help bridge the gap between evidence and clinical practice, supporting improved long-term survivorship outcomes.

1.3.3 Adipose Tissue Mass and Weight Gain Concern

Breast cancer survivors with high adipose tissue mass are at increased risk of recurrence and cardiovascular events, including those with a healthy body mass index (BMI) (101,155). This highlights the limitations of BMI as a stand-alone clinical tool; however, it remains the routine anthropometric measure used in oncology outpatient settings despite its inability to capture adiposity-related complications. Moving beyond the simplistic “eat less, move more” narrative is essential, as appetite regulation, body weight and energy balance are governed by

complex neurohormonal pathways involving gut-derived, adipose-derived and central signals (156), which may be further disrupted in hormone receptor–positive breast cancer by adjuvant endocrine therapies.

The Adapted Clinical Practice Guidelines for Ireland define obesity as a complex chronic disease characterised by excess or dysfunctional adiposity that impairs health (156). As a chronic condition, management requires long-term, comprehensive medical, functional, psychosocial and behavioural assessment rather than short-term weight reduction strategies. This is particularly relevant in breast and gynaecologic cancer survivorship, where treatment-related changes in body composition and elevated cardiometabolic risk require nuanced management approaches.

Understanding the current care context is critical. A 2024 scoping review (n = 5 studies; n = 113 participants) reported experiences of weight-based discrimination, stereotyping and internalised bias across the cancer continuum (157). During survivorship, this included unreasonable weight-loss directives, stigmatising language (e.g., use of “fat”), and internalised shame, with some individuals reporting disordered behaviours such as laxative use to meet perceived clinical expectations (157). In the Share Thoughts on Breast Cancer study (n = 1,198), women with obesity were less likely to rate their care as excellent or very good post-diagnosis ($p = 0.026$), although the underlying reasons require further investigation (158). Similarly, a qualitative study (n = 30; 15 breast, 15 cervical survivors) identified weight-centred discussions of recurrence and misconceptions regarding obesity, with participants reporting that weight-related assumptions influenced treatment decision-making (159). Collectively, these findings underscore the need for evidence-based, non-stigmatising communication around weight and recurrence risk in survivorship care.

Recent Irish obesity guidelines provide a more appropriate framework for this context, prioritising health-linked, patient-centred outcomes, sustainable behaviour change and multidisciplinary care rather than weight reduction alone (156,160). The Irish Nutrition and Dietetic Institute position paper similarly emphasises sustainable lifestyle change and multidisciplinary intervention models rather than traditional advice-giving approaches (161). Such frameworks offer practical implementation guidance that is largely absent from oncology-specific recommendations. While ESPEN and ESMO advise maintaining "*a healthy weight*" and "*avoid being overweight*", they provide limited direction on implementation within the complex physiological and psychosocial context of breast cancer survivorship (4,132).

Collectively, the evidence indicates that breast and gynaecologic cancer survivorship care requires integration of obesity-specific, patient-centred clinical frameworks, shifting emphasis from BMI thresholds and stigma-driven narratives toward strategies that optimise body composition, cardiometabolic health and long-term survivorship outcomes.

1.3.4 Bone Health

The European Food Safety Authority (EFSA) advise that in women over 50 years of age, at least 1200mg of calcium from all sources and or at least 1200mg of calcium and 800 IU of vitamin D from all sources to be consumed daily, and are considered for the purpose of reducing the risk of osteoporotic fractures by reducing bone mineral density (162). Females undergoing cancer treatment can experience accelerated bone loss, within six months of treatment, resulting in a substantial 21% decrease in bone density compared to age-matched menstruating females (79,80). Furthermore, postmenopausal breast cancer survivors prescribed an aromatase inhibitor and

gonadotropin-releasing hormone (GnRH) agonist experience bone loss at a yearly rate 7.7% higher than the general population (81) .

As per the ASCO and ESMO guidelines Calcium and Vitamin D supplementation of 1000mg and 800IU per day is recommended to support bone mineral density (4,163). Anecdotally, breast cancer survivors find the taste and texture of prescribed combined calcium and Vitamin D supplements "chalky" and often turn to over the counter supplements in pharmacies or health food stores. Ensuring that patients have access to acceptable alternatives is crucial for supporting bone health. The rising trends of plant-based dairy alternatives and organic food is a cause for concern, particularly when the nutritional value of these products is misunderstood. In Ireland, approximately 11% of adults aged 19-64 years and 7% of >65 years reported consuming non-dairy milk alternatives (145). If diets are not carefully planned, essential nutrients, like protein, iodine and calcium may be unintentionally excluded. For individuals who choose these alternatives working with a registered dietitian to carefully assess and plan their diet can help ensure they meet all their macro- and micro-nutrient requirements. In a systematic review investigating nutritional intakes in plant-based versus meat eaters (n = 141 studies) authors highlighted that whilst vegetarians had the highest intake of calcium from food sources (895mg; vs meat eaters 858mg; vs vegans 838mg), calcium was identified as a nutrient at risk of inadequacy (164). Authors noted that calcium absorption from plant-based sources may be reduced by phytates and oxalates from plant foods as well as insufficient intake of other macro- and micro-nutrients such as protein and vitamin D (164).

In the most recent National Adult Nutrition Survey II the mean intake of calcium amongst Irish females aged 19-64 years was 854mg (±336mg) per day and amongst

females >65 years was 1002mg (±381mg) which is lower than the EFSA recommendation (145,162). Furthermore, the intake of calcium from food sources was lower than recommended by EFSA: in females aged 19-64 years 795mg (±277mg) and aged >65 years 839mg (±289mg) (145). Another consideration must be made for women who experience an iatrogenic menopause at younger ages, such as those under 44 years of age. Using the NHANES II data, Miketinas et al. (2024) reported calcium intake of 981.2mg (±27.9mg) per day amongst women aged 20 – 44 years (n = 9,737 non-pregnant) (165). Particular note must be made for this cohort of women to ensure that they have adequate intake of calcium to mitigate the effects of iatrogenic menopause and/or adjuvant endocrine therapies on their bone health.

Looking towards breast cancer specific data, Xu et al. (2024) reported that in a small cohort of survivors (n = 97) 84% did not meet the recommended daily allowance for calcium, and a further 52.6% did not meet the recommended daily allowance for calcium with supplementation (166). Furthermore, in a larger Korean cohort (n = 701), non-supplement users reported a daily calcium intake of 580mg (±243.5mg) per day, and supplement users reported a marginally higher intake of 598.7mg (±279mg) per day (167).

Taken together, these findings highlight that despite clear recommendations calcium intake remains insufficient among many women, particularly breast cancer survivors, underscoring the need for tailored dietary guidance and accessible supplementation strategies to optimise bone health.

1.3.5 Gut Health

Optimising gut health through targeted nutritional strategies is an essential component of survivorship care for breast and gynaecologic cancer survivors experiencing iatrogenic menopause as diet plays a pivotal role in modulating the gut microbiome, supporting digestive function, and enhancing overall well-being. Of the various nutritional factors influencing gut health, dietary fibre is particularly important, given its role in regulating bowel function, alleviating treatment-related gastrointestinal disturbances, and contributing to cardiometabolic protection in this cohort.

Dietary fibre intake remains consistently below recommendations (25g-32g/day in Europe), with mean intakes across 21 European surveys averaging 19 g/day (range 13g-26g) (168,169). In Ireland, women aged 19 to 64 years and >65 years consume approximately 17g/day (±5.6g; ±5.5g respectively), highlighting a persistent population-level deficit (145). This shortfall is clinically relevant in survivorship, where gastrointestinal symptoms, cardiometabolic risk, and systemic inflammation are common.

Dietary fibre modulates the gut microbiota through colonic fermentation, promoting short-chain fatty acid production and supporting immune and metabolic function (170). A meta-analysis (n = 64 studies; n = 2,099 participants) demonstrated that fructans and galacto-oligosaccharides increase faecal Bifidobacterium and Lactobacillus spp., strains associated with health-promoting effects (170,171). In cancer populations, a 2021 systematic review (n = 12 studies; n = 974 participants) reported significant improvements in abdominal pain ($p = 0.001$), irritable bowel syndrome symptoms ($p = 0.03$), diarrhoea ($p = 0.03$), constipation ($p < 0.05$), anxiety and depression ($p = 0.01$), and colorectal cancer–related quality of life ($p = 0.04$) with fibre-related interventions (172).

Special consideration is required for survivors who have received pelvic radiotherapy. Chronic radiation-induced bowel changes may impair absorption and increase diarrhoea, flatulence, and malnutrition risk (44,173). A 2018 Cochrane review (n = 92 studies) evaluating non-pharmacological interventions for gastrointestinal toxicity found dietary modification evidence to be of low or very low certainty, concluding that ongoing multidisciplinary nutritional monitoring remains essential (44).

Beyond symptom management, fibre intake is strongly associated with long-term health outcomes. An umbrella review (n = 18 meta-analyses; median n = 342,437 participants) reported statistically significant protective associations in 86% of outcomes examined (174). A recent systematic review (n = 64 studies; n = 3,513,828) demonstrated that higher fibre intake reduced all-cause mortality by 23% (*HR 0.77; 95% CI 0.73 to 0.82*), cardiovascular mortality by 26% (*HR 0.74; 95% CI 0.71 to 0.77*), and cancer mortality by 22% (*HR 0.78; 95% CI 0.68 to 0.87*) (175)

Taken together, the evidence highlights dietary fibre as a cornerstone of nutritional care for breast and gynaecologic cancer survivors experiencing iatrogenic menopause, with benefits extending beyond gut health to cardiometabolic protection, symptom management, and reductions in long-term morbidity and mortality though individualised guidance remains essential given treatment-related gastrointestinal vulnerabilities.

1.3.6 Heart Health

Diet is a key modifiable risk factor for cardiovascular disease, particularly in individuals who have undergone radiotherapy or iatrogenic menopause (176).

Adherence to Mediterranean-style eating, emphasising nutrient-dense, plant-forward foods, has been robustly linked to reduced cardiovascular risk. A 2014 meta-analysis, including 4.17 million participants, associated adherence to this style of eating with 8% reduction of overall mortality (*relative risk (RR)= 0.92; 95 % CI 0.91 to 0.93*) and a 10% reduced risk of cardiovascular disease (*RR = 0.90; 95 % CI 0.87 to 0.92*) (177). This meta-analysis included data from large randomised controlled trials such as CORonary Diet Intervention with Olive oil and cardiovascular PREVention (*CORDIOPREV*) study (178); the PREvencion con DIeta MEDiterranea (*PREDIMED*) trial (179); the Lyon Diet Heart Study (180); Dietary Approaches to Stop Hypertension (*DASH*) trial (181); and the Portfolio Diet (182). Each emphasises nutrient-dense, plant-forward eating, but they differ in design and therapeutic focus.

Overall, extensive evidence supports the Mediterranean style of eating as a highly effective strategy for reducing cardiovascular risk and promoting longevity which is particularly important in breast and gynaecologic cancer survivors experiencing iatrogenic menopause, who face heightened vulnerability to heart disease.

1.4 DIETARY QUALITY SCORES

Dietary quality scores have become increasingly important in cancer survivorship research offering a way to assess overall dietary patterns rather than isolated foods or nutrients. These scores are particularly relevant for survivors experiencing iatrogenic menopause, where changes in body composition, and chronic disease risk may increase vulnerability to adverse health outcome and cancer recurrence. This section examines three prominent dietary scores - the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) dietary score, Mediterranean diet scores, and the MIND (Mediterranean-DASH Intervention for Neurodegenerative Delay) diet

score, and their applicability to cancer survivors. Each score provides a structured approach to evaluating adherence to dietary patterns that may mitigate long-term treatment-related risks and promote overall well-being during survivorship. Moreover, these scores offer practical guidance for designing dietary interventions aimed at improving health outcomes and quality of life in this vulnerable population.

Despite the increasing use of dietary quality scores in research clinical practice appears to reflect a more nuanced reality. Dietitians often focus on nutrient targets like energy and protein rather than whole dietary patterns and their familiarity with patterns such as the Mediterranean diet varies (183). A recent qualitative study revealed that recommendations may emphasise meal timing, frequency and variety over formal patterns, particularly during acute treatment, however they may play a more meaningful role during cancer survivorship to support long-term health and reduce recurrence risk (183). By incorporating these insights, dietary quality scores can serve as a bridge between research and practice, offering a structures framework that supports dietitians in translating dietary pattern evidence into meaningful, patient-centred recommendations across the cancer continuum.

1.4.1 World Cancer Research Fund Recommendations Dietary Quality Score

The World Cancer Research Fund (WCRF) is an international organisation focused on reducing the global burden of cancer through rigorous research, public engagement and the development of evidence-based recommendations. The Global Cancer Update Programme is the flagship research initiative from the WCRF, in partnership with the American Institute for Cancer Research (AICR). The key aims of research within the Global Cancer Update Programme from the WCRF are to develop population or disease-specific guidance and recommendations; the clarification of existing

knowledge for greater understanding of cancer prevision and survivorship; globally representative research; inclusion of strong public involvement; the use of varied and targeted outputs; global collaborators and expert and stakeholder input; as well as keeping evidence current with efficient and targeted approaches. It systematically reviews and analyses evidence on how diet, nutrition, physical activity and body weight affect cancer risk and survival. Its main purpose is to continuously update and evaluate evidence linking lifestyle facts to cancer, ensuring that their Cancer Prevention Recommendations remain current and evidence based. The database includes more than 12,000 studies, with contributions from over 140 scientists across more than seventeen countries.

The programme uses a four-step method to review and determine new guidance and recommendations: (1) scope and prioritise evidence; (2) complete systematic literature reviews; (3) grade the evidence; and (4) form the guidance and recommendations (244). The current body of work by the WCRF is categorised into four areas: cancer incidence; cancer survivors; cancer mechanisms; and obesity.

The programme has released two initial reports for cancer survivors, specifically targeting breast (184) and colorectal (185) cancers. Whilst the WCRF has not released any specific recommendations for cancer survivors, due to a limited evidence, they have advised that cancer survivors follow the Cancer Prevention Recommendations as far as possible following the acute treatment stage (186).

In 2018, the World Cancer Research Fund International published "*Diet, Nutrition, Physical Activity and Cancer: A Global Perspective*", it's third expert summary report. In a shift from the 2007 *Expert Summary Report* the third summary focused on a holistic approach, acknowledging that it is increasingly unlikely that specific foods,

nutrients or other component of foods themselves cause or prevent cancer (186). Instead, the report emphasised that various patterns of diet and physical activity interact to create a metabolic state that can either favour or hinder the genetic and epigenetic changes responsible for the cellular structural and functional alterations underlying the principal mechanisms of cancer progression (186). In summary, the WCRF highlights that whilst following each individual recommendation will be of benefit in relation to cancer protection most benefit is gained from treating all ten recommendations as an over-arching package (186).

There are ten recommendations for cancer prevention, as outlined in Table 1.5, that are also deemed to be suitable for cancer survivorship (186).

Together, the WCRF's recommendations offer an integrated framework linking lifestyle to cancer prevention and survivorship, forming the basis for the development and operationalisation of the cancer prevention and survivorship score.

1.4.1.1 Development and Operationalisation of the WCRF Dietary Quality Score

Following the publication of the 2007 Expert Summary Report and the WCRF/AICR Cancer Prevention Recommendations researchers developed their own scores based on the adherence to the recommendations to investigate associations with cancer risk and health outcomes (187–206). The studies reported that greater adherence was associated with reduced risk and incidence of general and site-specific sources (188–190,192,194,195,197,199–201,205–207), and reduced all-cause and cancer-specific mortality (191,193,196,198,202–204).

Table 1.5: Summary of 2018 WCRF/AICR Dietary Quality Score

Recommendation	Goals of Recommendation	Operationalisation of Recommendations	Score
1. Be a healthy weight	Keep your weight as low as you can within the healthy range throughout life. Avoid weight gain throughout adulthood (measured as body weight or waist circumference)	**BMI** 18.5–24.9 25–29.9 <18.5 or ≥30 **Waist Circumference** Women: <80 (<31.5) Women: 80–<88 (31.5– <35) Women: ≥88 (≥35)	 0.5 0.25 0 0.5 0.25 0
2. Be physically active	Be at least moderately active, and follow or exceed national guidelines Limit sedentary habits	**Total Moderate-Vigorous Physical Activity (minutes / week)** ≥150 75 – <150 <75	 1 0.5 0
3. Eat a diet rich in wholegrains, vegetables, fruit and beans	Consume a diet that provides at least 30g per day of fibre from food sources Foods containing wholegrains, non-starchy vegetables, fruit and pulses Eat at least five portions of a variety of plant foods per day (400g total)	**Fruits and vegetables (g/day):** ≥400 200 – <400 <200 **Total fibre (g/day):** ≥30 15 – <30 <15	 0.5 0.25 0 0.5 0.25 0
4. Limit fast food / ultra-processed foods	Limit consumption of processed foods high in fat, starches or sugars – including fast foods, many prepared dishes, snacks, bakery foods, desserts and confectionary	**Percentage of total kcal from ultra-processed foods** Tertile 1 Tertile 2 Tertile 3	 1 0.5 0
5. Limit consumption of red and processed meat	Limit red meat to no more than three portions per week (350g – 500g cooked weight) Consume very little, if any, processed meat	**Total red meat (grams/week) and processed meat (grams/week):** Red meat <500 and processed meat <21 Red meat <500 and processed meat 21– <100 Red meat >500 or processed meat ≥100	 1 0.5 0
6. Limit consumption of sugar-sweetened drinks	Do not consume sugar sweetened drinks	**Total sugar-sweetened drinks (grams/day):** 0 >0 – ≤250 >250	 1 0.5 0
7. Limit alcohol consumption	For cancer prevention, best not to drink alcohol	**Total ethanol (grams/day):** 0 ≤14 (1 drink) females >14 (1 drink) females	 1 0.5 0
8. For mothers: breastfeed your baby, if you can	Along with WHO advice, infants should be exclusively breast fed for 6 months and then up to 2 years or beyond alongside complementary feeding	**Exclusively breastfed over lifetime for a total of:** 6+ months >0 – <6 months Never	 1 0.5 0

Whilst a positive move forward in the area the scores varied considerably in the number of recommendations used within the scores as well as the cut points derived to determine adherence scores for each recommendation (187). Given this, in 2019, a joint effort between the US National Cancer Institute and members of the WCRF (International) and AICR, with consultation from the Global Continuous Update Programme led to the development of a standardised scoring system of the WCRF Cancer Prevention Recommendations (187).

The score, as presented in Table 1.5, is comprised of eight components for females. Two of the ten recommendations were excluded from the score following review: dietary supplementation and the use of the prevention score for cancer survivors (187). The authors reported that five of the recommendations addressed that the majority of nutrients should be derived from foods and not supplementation, and that the use of the score for cancer survivors may double-count the impact of adherence (187).

To develop the overall cut points for the score, the authors consulted those explicitly noted in the 2018 WCRF Summary Report, and guidelines from the Centres for Disease Control and Prevention and the World Health Organisation, as well as reviewing the cut points utilised in the aforementioned studies using the 2007 WCRF Recommendations (187). This resulted in a three-level scoring system of eight recommendations, with a maximum score of eight (Table 1.5). It was acknowledged that partially meeting a recommendation, for example consuming 15g - <30g of fibre of day, may still provide some benefit compared to not meeting the recommendation at all (187). For recommendations such as "*Be a healthy weight*" and "*Eat a diet rich in wholegrains, vegetables, fruit and beans*", the scoring system was divided to account for the sub-operations such as body mass index and waist circumference.

Equal weight is given to each sub-operation using the three-level scoring system, to meet a total score of one (Table 1.5).

1.4.1.2 Validation and the Use of WCRF Dietary Quality Score in Research

Several large-scale prospective cohort studies and meta-analyses have validated the WCRF/AICR dietary quality score as a robust predictor of cancer risk across diverse populations, demonstrating consistent inverse associations with cancer incidence and highlighting its utility in nutritional epidemiology.

In the NutriNet-Santé cohort (n = 41,543), the WCRF dietary quality score was calculated from three dietary assessments picked over two weekdays and one weekend day using an online validated 24 hour dietary record (208). Dietary intake was correlated with blood and urinary markers, and compared with an interview from a trained dietitian (208). The average WCRF score was 4.8 ±1.1, and findings highlighted that a one point increased in adherence to the score was associated with a decreased overall, breast and prostate cancer risk (12%, *95% CIs 8% to 16%, $p < 0.0001$;* 14%, *95% CIs 6% to 21%, $p = 0.001$;* 12%, *95% CI 0% to 22%, $p = 0.05$*).

Similarly, in the UK Biobank Study (n = 94,778) authors assessed adherence to the dietary score but also included modifications to the score (209). Modifications included expanding the body weight recommendation to include sub score for body fat percentage and a body shape index, as well as modifications to the physical activity and red meat recommendation score cut points to align with evidence for optimal health (209). The mean score was 3.84 ± 1.0, slightly lower than the NutriNet-Santé cohort (209). Findings from the original score, with no modifications, similarly reported that each one point increase in adherence was associated with a 7% lower

cancer risk (*HR = 0.93, 95% CIs 0.90 to 0.95, p < 0.001*) (209). Authors did not disclose what methods were used to collect dietary intake (209).

In a meta-analysis of seven cohort studies (n = 361,616), all cohorts reported using a validated food frequency questionnaire to collect dietary intake (194). Consistent with previously reported literature findings highlighted that a one-point increase in adherence to the dietary quality score was significantly associated with a 6% lower risk in cancer in individuals > 60 years (*HR 0.96, 95% CIs 0.93 to 1.00*) (194).

While these findings demonstrate the predictive utility of the WCRF/AICR dietary quality score across diverse cohorts, differences in dietary assessment tools, score modifications, and reporting methods raise important methodological considerations. Such variability is central to interpreting findings as differences in dietary assessment approaches and population-specific adaptations can affect both the reliability and comparability of results across studies (Table 1.6). The most common tool was the food frequency questionnaire (FFQ) though several cultural and cohort-specific adaptations were employed (210–213). Overall, this methodological heterogeneity underscores the need for greater standardisation to enhance validity, reliability, and comparability of WCRF/AICR dietary quality score research. In light of this, examining the strengths and limitations of the dietary assessment tools themselves is essential for understanding their influence on study outcomes.

Table 1.6: Variability in Dietary Assessment Tools Used in Studies Investigating WCRF/AICR Adherence

Study	Country	Participants	Dietary Assessment Tool(s) Used
UK Biobank Malcomson et al. 2023 (214)	United Kingdom	94,778	• Short FFQ based approach (28 questions on diet, 18 questions on alcohol) • Four 24-hour dietary recalls completed at home, using web-based platform (mean of 2 dietary assessments were used).
El Kinay et al. 2019 (210)	Morocco	3,022	• Validated semi-quantitative food frequency questionnaire adapted for the Moroccan context • Assisted by a trained interviewer
NIH-AARP Diet and Health Study Shams-White et al. 2022 (213)	United States of America	177,410	• NIH-AARP 124 food item questionnaire
Health-Examinees Gem Study Lee et al. 2023 (211)	Korea	104,386	• 106 food item semi-quantitative FFQ
Won et al. 2024 (212)	Korea	5,485	• 106 food item semi-quantitative FFQ
Gali et al. 2023 (215)	Germany	8,584	• EPIC FFQ
Gavioli et al. 2025 (216)	Netherlands	3,668	• 10 item self-administered questionnaire
Systematic Review and Meta Analysis Malcomson et al. 2023 (214)	Multiple	1,170,705 *18 independent studies reported*	• Self-administered touchscreen questionnaire • Self-reported FFQ • Interviews for FFQ • Face to face interviews including questionnaire for diet

Abbreviations: FFQ Food Frequency Questionnaire, EPIC European Prospective Investigation into Cancer, NIH-AARP National Institutes of Health American Association of Retired Persons

The use of dietary assessment tools is dependent on the scope of interest of the research, including study design and research questions (217). For example, investigations interested in the whole diet would use 24-hour dietary recalls and food frequency questionnaires, whereas those interested in one or a few components would use a screener or food frequency questionnaire (217).

Furthermore, when focussing on study design interventional studies preferably used 24-hour recalls, food frequency questionnaires and screeners, whereas prospective studies include the use of food records as well (217). It must be acknowledged that all dietary assessments are subject to measurement error (217,218). There are two types

of measurement error: random and systematic (217). Random measurement error refers to within person day to day variation whereas systematic error refers to the tendency of the interviewee to underreport or overreport foods, secondary to social desirability (217). Both of these errors can impact the accuracy of dietary assessment tools.

Shim et al. (2014) reports on the dietary assessment tools used in epidemiological research, including those used when assessing adherence to WCRF/AICR Dietary Quality Score (218). Common limitations include recall bias and low accuracy, large respondent burden and healthcare professional burden and lack of clinical translation of tool due to specificity to research population (218).

In summary, while the WCRF/AICR dietary quality score consistently demonstrates predictive value for cancer risk the accuracy and comparability of findings are largely contingent on the dietary assessment tools employed, underscoring the need for standardised, validated methods to strengthen future research

1.4.1.3 The Discourse around Ultra-Processed Foods

Ultra-processed foods (UPFs) are defined primarily by industrial processing rather than nutrient content, and the NOVA classification has been criticised for inconsistency, lack of nuance, and potential to mislead both consumers and health professionals (219–222). Media and social discourse frequently overgeneralise UPFs as “unhealthy” or “junk food,” further confounding public understanding (223–225). For populations such as cancer survivors, where nutrient adequacy is critical, these limitations reduce the utility of UPFs as a standalone dietary measure (225). Consequently, the UPF component was removed from Chapter 4, with broader

dietary quality scores providing a more evidence-based, nutrient-focused assessment while still acknowledging processing considerations.

While the WCRF/AICR dietary quality score offers a robust evidence-based framework the NOVA classification exposes gaps in both scientific classification and public communication. These issues underscore the need for approaches that integrate nutrient content with processing considerations and provide clear, evidence-driven guidance to support informed, balanced dietary practices in breast and gynaecologic cancer survivorship.

1.4.2 Mediterranean Dietary Quality Score

Current nutrition guidelines for breast and gynaecologic cancer survivorship remain largely generic, contributing to uncertainty regarding the role of diet in post-diagnosis survival and symptom management (226). The European Society of Clinical Nutrition and Metabolism recommends a healthy lifestyle for cancer survivors, including regular physical activity and a diet rich in vegetables, fruits, and whole grains, and low in saturated fat, red meat, and alcohol (132). These align closely with WCRF Recommendations for Cancer Prevention (186) and follow similar principals to the Mediterranean diet (MedD). In addition, the MedD has been endorsed by the European Society of Menopause and Andropause for the management of menopausal symptoms and long-term health (140), underscoring its relevance for breast and gynaecologic cancer survivors.

The MedD is characterised by high intakes of plant-based, polyphenol-rich foods and low consumption of pro-inflammatory foods, such as processed products and red meat (227,228). Its benefits appear to arise from the overall dietary pattern rather than individual components (229). Adherence to the MedD has been associated with

reduced breast cancer risk and improved outcomes across a range of chronic conditions, including cardiovascular disease, osteoporosis, diabetes, obesity, and metabolic syndrome (230–236), suggesting potential benefits beyond current cancer-specific dietary guidance.

Adherence to the MedD is commonly assessed using dietary quality scores; however, considerable variation exists across scoring tools in terms of components, scoring methods, and adherence thresholds, limiting comparability across studies (237). This lack of standardisation also contributes to the limited uptake of MedD adherence assessment in clinical practice (238,239). Nevertheless, MedD adherence scores may offer a practical indicator of overall dietary quality and provide a useful framework for dietary modification to support symptom management and long-term health in breast and gynaecologic cancer survivorship.

MedD adherence scores reported in the literature vary widely, reflecting differences in study populations, survivorship stages and assessment timing, from post-treatment to long-term follow-up. Most research includes women with stage 0–III breast cancer, but adherence by tumour subtype is rarely examined. Overall, the literature shows substantial variability and highlights gaps in stratified and longitudinal analyses.

Several tools have been used to assess adherence to the MedD, reflecting variation in how dietary recommendations are operationalised across studies (Table 1.7). Across the available literature eight different MedD scoring tools were employed, most commonly the 14-item Mediterranean Diet Adherence Screener (MEDAS) (226,240–245). Other tools included modified versions of the Alternate Mediterranean Diet score (246), MEDI-LITE (247), the Mediterranean Diet Score (248), MedDiet (249), a cardioprotective Mediterranean Diet score (250), and the Italian Mediterranean Diet

Index (251,252). Although these tools consistently promote higher intakes of vegetables, fruits, legumes, fish, olive oil, and nuts, and discourage red and processed meats, sugary foods, and high saturated fat intake, they differ substantially in scoring methods, component selection, and adherence thresholds (237). Some tools use binary scoring, while others apply frequency-, median-, or portion-based cut-offs, and several have been adapted for specific populations or intervention contexts (237,238). This lack of standardisation limits cross-study comparability and complicates interpretation of adherence levels in breast cancer survivorship research.

Despite heterogeneity in MedD scoring tools most intervention studies report improvements in adherence following dietary intervention. Of the studies assessing pre- and post-intervention adherence the majority observed statistically significant increases in MedD scores (226,240–243,245,247,249), indicating that Mediterranean-style dietary patterns are achievable in breast cancer survivors in the short term. However, the magnitude of improvement varied across studies and not all interventions demonstrated significant change (252).

Increased overall adherence was commonly accompanied by favourable changes in individual dietary components, including higher intakes of vegetables, legumes, fish, and olive oil, alongside reduced consumption of red and processed meats and sweets (241,250,251). These findings suggest that dietary behaviour change aligned with MedD principles is feasible, although evidence on long-term adherence remains limited.

Evidence examining clinical outcomes associated with MedD adherence in breast cancer survivors remains limited. One large prospective cohort reported no association between MedD adherence and breast cancer–specific mortality or recurrence, although

lower all-cause mortality was observed among women with lower levels of physical activity (246). Broader evidence from non-cancer populations supports an inverse association between MedD adherence and all-cause mortality, but highlights the need for consistent adherence measurement to strengthen survival estimates (253,254).

Across intervention studies MedD adherence was generally associated with modest improvements in anthropometric and metabolic outcomes, including reductions in body weight, BMI, waist circumference, and markers of glycaemic control (226,240,242–245,251). Effects on lipid profiles and inflammatory markers are mixed, with some studies reporting favourable changes and others observing no significant effects (226,243,245,248,252). Variability in follow-up duration, baseline metabolic status, and intervention design likely contributes to these inconsistencies.

Evidence linking MedD adherence to quality-of-life outcomes in breast cancer survivors is inconsistent. Some intervention studies report improvements in physical functioning, fatigue, and global health status (240,244) while others find no significant associations between adherence and quality-of-life measures (226,241). A recent systematic review similarly reported mixed findings regarding MedD adherence and quality-of-life outcomes in breast cancer populations (253).

Evidence from non-cancer populations suggests potential cognitive and psychosocial benefits of Mediterranean-style dietary patterns, likely mediated through anti-inflammatory and cardiometabolic pathways (154,255,256). However, robust evidence linking MedD adherence to sustained quality-of-life improvements in breast cancer survivorship remains limited.

The existing evidence base is characterised by several methodological limitations. Most studies rely on self-reported dietary intake, introducing recall and social desirability bias. Comparability across studies is further limited by the absence of standardised MedD scoring tools and inconsistent operationalisation of dietary components (237,238). Short intervention durations and small sample sizes constrain the assessment of long-term adherence and clinically meaningful outcomes. In addition, adjustment for key confounders and use of objective biomarkers to validate dietary adherence were uncommon, limiting the strength of causal inference.

Emerging evidence suggests Mediterranean dietary patterns may support diet quality and cardiometabolic health after breast cancer treatment, but current findings are insufficient for clinical recommendations. Future research should focus on well-powered, longitudinal studies using standardised, culturally adapted MedD scoring tools. While the MedD offers a potentially integrative framework for addressing treatment-related metabolic changes and chronic disease risk, formal validation of assessment tools and evaluation of long-term outcomes are needed before routine clinical implementation can be justified.

Table 1.7: Specific Components of Mediterranean Dietary Score and Operationalisation of Recommendations

Mediterranean Dietary Component	Mediterranean Dietary Scores and Operationalisation of Recommendations																	
	Cardioprotective Mediterranean Diet Score *Martinez-Gonazales et al. 2004* (257)		**MEDAS 14 ^** *Schnoder et al. 2011* (256)		**aMED** *Kim et al. 2011* (246)		**Mediterranean Diet Score** *Demetriou et al. 2012* (258)		**MEDI-LITE** *Sofi et al. 2013* (177)		**Italian Mediterranean Index** *Agnoli et al. 2013* (259)		**Modified MEDAS 14** *Cho et al. 2020* (244)		**PREDIMED-PLUS Energy Restricted** *Martinez-Gonazales et al. 2019* (260)	
Vegetables	✓	1 point = ≥ 1 servings/day Additional point if ≥ 1 serving/day of vegetables *and* fruit	✓	1 point = ≥ 2 servings/day	✓	1 point if > median intake	✓	1 point if ≥ 1 serving/day Additional point if ≥ 1 serving/day of vegetables *and* fruit	✓	0 = <1 portion/day 1 = 1-2.5 portions/day 2 = >2.5 portions/day	✓	1 point if > third tertile of distribution	✓	1 point = ≥ 2 servings/day	✓	1 point = ≥ 2 servings/day (≥1 portion raw or in a salad)
Legumes / Pulses	✓	1 point = ≥ 2 servings/week	✓	1 point = ≥ 3 servings/week	✓	1 point if > median intake	✓	1 point if ≥ 2 servings/week	✓	0 = <1 portion/week 1 = 1-2 portions/week 2 = >2 portions/week	✓	1 point if > third tertile of distribution	✓	1 point = ≥ 3 servings/week	✓	1 point = ≥ 3 servings/week
Fruits	✓	1 point = ≥ 1 servings/day Additional point if ≥ 1 serving/day of vegetables *and* fruit	✓	1 point = ≥ 3 pieces/day	✓	1 point if > median intake	✓	1 point if ≥ 1 serving/day Additional point if ≥ 1 serving/day of vegetables *and* fruit	✓	0 = <1 portion/day 1 = 1-1.5 portions/day 2 = >2 portions/day	✓	1 point if > third tertile of distribution	✓	1 point = ≥ 3 servings /day	✓	1 point = ≥ 3 servings /day
Wholegrains / Cereals	✓	1 point = white bread <1 serving per day and rice <1 servings per week *or* wholegrain bread >5 servings per week			✓	1 point if > median intake (only wholegrains included)	✓	1 point if 1-3 serving/day	✓	0 = <1 portion/day 1 = 1-1.5 portions/day 2 = >1.5 portions/day	✓	1 point if intake of pasta is > third tertile of distribution			✓	1 point = ≤1 serving of white bread per day 1 point = ≥5 times per week of wholegrain cereals and pasta 1 point = <3 times per week of non-whole grain pasta or white rice
Potatoes											✓	1 point in intake is < 1st tertile of distribution				
Fish / Seafood	✓	1 point = ≥ 3 servings/week	✓	1 point = ≥ 3 servings/week	✓	1 point if > median intake	✓	1 point if ≥ 3 servings/week	✓	0 = <1 portion/week 1 = 1-2.5 portions/week 2 = >2.5 portions/day	✓	1 point if > third tertile of distribution	✓	1 point = ≥ 3 servings/week	✓	1 point = ≥ 3 servings/week
Poultry / Lean Meats	✓	1 point = < 1 serving/day *	✓	1 point if white meat is preferred over red meat			✓	1 point if < 1 serving/day +	✓	0 = >1.5 portion/day 1 = 1-1.5 portions/day			✓	1 point if white meat is preferred over red meat	✓	1 point if white meat is preferred over red meat

Red Meat			✓	1 point = < 1 serving/day *	✓	1 point if < median intake *				2 = <1 portion/day +	✓	1 point in intake is < 1st tertile of distribution	✓	1 point = < 1 serving/day *	✓	1 point = < 1 serving/day *
Processed Meats													✓	1 point = < 1 serving/day *	✓	1 point = < 1 serving/day *
Dairy					✓	1 point if < median intake			✓	0 = <1.5 portion/day 1 = 1-1.5 portions/day 2 = <1 portion/day						
Butter / Cream / Margarine			✓	1 point = < 1 serving/day of animal fat							✓	1 point in intake of butter is < 1st tertile of distribution	✓	1 point = < 1 serving/day	✓	1 point = < 1 serving/day
Olive Oil			✓	1 point if used as primary cooking fat 1 point if ≥ 4 tbsp/day	✓	1 point if ratio of monounsaturated fat to saturated fat is > median ration	✓	1 point if ≥ 1 spoon/day	✓	0 = occasional use 1 = frequent use 2 = regular use	✓	1 point if > third tertile of distribution	✓	1 point if used as primary cooking fat 1 point if ≥ 4 tbsp/day	✓	1 point if extra virgin olive oil is primary oil used for cooking, spreads and salad dressings
Nuts			✓	1 point = ≥ 3 servings/week									✓	1 point = ≥ 3 servings/week	✓	1 point = ≥ 3 servings/week
Tomato / Onion / Leek Sauce			✓	1 point if ≥ 2 servings/week									✓	1 point if ≥ 2 servings/week	✓	1 point if ≥ 2 servings/week
Dessert / Sweets																
Commercial Cakes			✓	1 point if < 2 per week									✓	1 point if < 3 per week	✓	1 point if < 3 per week
Fizzy Drinks / Sugar Sweetened Soft Drinks			✓	1 point if < 1 cup/day (100 ml)							✓	1 point in intake is < 1st tertile of distribution	✓	1 point if < 1 drink/day (100 ml)	✓	1 point = <1 sugary beverages or sugar-sweetened fruit juices per week 1 point if avoid adding sugar to beverages
Alcohol	✓	1 point = ≥ 1 glass per day	✓	1 point if ≥ 7 servings/week of red wine	✓	1 point = 5 -15g/day	✓	1 point if zero consumption	✓	0 = >2 AU/day 1 = <1 AU/day 2 = 1-2 AU/day	✓	1 point = ≤12 g/day 0 point = <12g/day or abstainers			✓	1 point = 1-2 glasses of wine per day
Maximum Score		9		14		9		9		18		11		13		17

* Red meat and processed meat included together.
+ All meat products included in score
^ The following studies included in this scoping review used the MEDAS 14 scoring tool to assess MedD adherence: Alvarez-Bustos et al. 2021; Braakhuis et al. 2017; Kwon et al. 2020; Natalucci et al. 2021; Ruiz-Vozmediano et al. 2020; Zeppa et al. 2023

1.4.3 Mediterranean-DASH Diet Intervention for Neurodegenerative Delay (MIND) Dietary Quality Score

The MIND (Mediterranean-DASH Diet Intervention for Neurodegenerative Delay) dietary quality score combines elements of the Mediterranean and DASH diets, prioritising foods linked to neuroprotection, including green leafy vegetables, berries, whole grains, nuts, beans, fish, and poultry, while limiting red meat, butter, cheese, pastries, and fried foods (261).

The 15-point MIND score integrates Mediterranean and DASH components and standardises servings based on a traditional Greek Mediterranean diet (261). In the Memory and Aging Project (n = 960, median follow-up 4.7 years), higher MIND adherence was significantly associated with better episodic memory ($p = 0.003$), semantic memory ($p = 0.007$), and perceptual speed ($p = 0.0002$) (261). A meta-analysis (n = 8 studies, n = 26,103) found that a one-standard deviation increase in MIND adherence corresponded to a 0.042-unit higher global cognitive z-score (*95% CI: 0.020 to 0.065*) and 0.010 units slower annual cognitive decline (*95% CI: -0.001 to 0.021*) (255).

Cognitive decline is common in breast and gynaecologic cancer survivors due to surgical or treatment-induced menopause, affecting verbal memory, semantic memory, processing speed, executive function, and visual memory (67,68). In a 2025 cross-sectional study of postmenopausal breast cancer survivors (n = 21), higher MIND adherence was linked to improved global cognitive score ($p = 0.013$), episodic memory ($p = 0.019$), attention/working memory ($p = 0.024$), and phonemic fluency ($p = 0.002$), with higher vegetable, legume, and lower red meat and “fast food” intake driving benefits (262).

While direct evidence in cancer survivors is limited, the MIND diet aligns with Mediterranean dietary patterns and existing survivorship recommendations, supporting cognitive and cardiometabolic health and potentially mitigating treatment- and menopause-related cognitive decline.

Collectively, these dietary quality scores offer a validated, evidence-based framework for assessing overall dietary patterns, with adherence consistently associated with reduced cancer risk, improved cardiometabolic profiles, and better cognitive outcomes, highlighting their potential utility in guiding dietary strategies to support long-term health and survivorship in women affected by breast and gynaecologic cancers.

1.5 FOOD SUPPLEMENTS: DIETARY AND HERBAL BOTANICAL SUPPLEMENT USE IN CANCER SURVIVORS

In addition to whole-diet patterns such as the MedD, many breast cancer survivors also use food supplements in an effort to improve recovery, manage symptoms, or reduce recurrence risk. This section outlines definitions, regulatory frameworks and patterns of use to contextualise subsequent analysis.

1.5.1 Definition

The European Food Safety Authority define a "food supplement" as "*any concentrated sources of nutrients, e.g. vitamins or minerals, or other substances with a nutritional or physiological effect that are marketed in dose form*". The "dose" form encompasses pills, tablets, capsules or liquids in measured doses. Food supplements may also contain other ingredients, not just one sole nutrient, including additional vitamins, minerals, amino acids, essential fatty acids, fibre and various plant, herbal and botanical extracts.

The United States Food and Drug Administration (FDA) defines "dietary supplements" as a product that is intended to add or supplement the diet, differing from conventional food (263). Dietary supplements, as per the FDA, are classed as a drug if the product is intended to treat, diagnose, cure or prevent diseases, even if labelled a dietary supplement (263). Dietary supplements include vitamins, minerals, botanicals or herbs, botanical compounds, amino acids and live microbials (263). The supplement can be ingested and comes in tablet, capsule, soft gel, gel caps, powders, bars, gummies or liquid forms (263).

In Australia and New Zealand, unlike Europe and the United States, "dietary supplements" are not officially recognised as a distinct regulatory category. Products that are commonly referred to as "dietary supplements" in other countries, such as Ireland, are regulated as either as "complementary medicines" by the Therapeutic Goods Administration (264) or as "foods" under Food Standards Australia New Zealand, depending on their composition and intended use (265).

In Ireland, the definition of a "food supplement" falls under the European Food Safety Authority definition (266,267).

1.5.2 Guidelines

The European Society of Clinical Nutrition and Metabolism (ESPEN) practical guideline on Clinical Nutrition in Cancer discourage the use of high-dose micronutrients in the absence of specific deficiency (132). The World Cancer Research Fund's Recommendations for Cancer Prevention, and Survivorship does not support the use of supplements for cancer prevention or as a means of improving survival (186). Furthermore, that National Comprehensive Cancer Network and the

American Society for Clinical Oncology caution the overuse and misuse of dietary supplements following the completion of anti-cancer treatment (268,269).

Special considerations for the use of dietary supplementation are required in hormone receptor positive breast cancer treated with adjuvant endocrine therapy, such as tamoxifen and aromatase inhibitors. The American Society of Clinical Oncology and the European Society of Medical Oncology recommend adequate vitamin D and calcium supplementation during adjuvant endocrine therapy, particularly aromatase inhibitor therapy due to its impact of bone mineral density and bone loss (270,271).

1.5.3 Regulation

In Europe, food supplements are considered foodstuffs and therefore, regulated according to the EU General Food Law Regulation (EC) No 178/2002 (272) and the Directive 2002/46/EC (273). The responsibility for the safety of food supplements lies with the food business operation who places the product on the market (272). The Directive has established a list of vitamins and mineral substances used in the manufacture of food supplements and the labelling requirements for these products. It aims to harmonise the laws between European Union member states concerning food supplements to ensure consumer safety and facilitate the free movement of these products within the European Union.

Any nutrition or health claims that are made about food supplements must comply with Regulations (EC) No 1924/2006 on nutrition and health claims made on foods (219).

The Heads of Food Safety Agency In Europe established a Working Group on Food Supplements to create a common approach on to the management and assessment of ingredients or nutrients that could pose a risk to public health when used in food

supplements (275). The group evaluated over 117 dietary supplements and identified thirteen as potential health risks, these included maca root, ashwagandha, tea tree oil, curcumin, tryptophan, black cohosh and melatonin (275). These substances could face restrictions, bans, or further evaluation by the European Food Safety Authority (EFSA), with final decisions expected in the coming years. The goal is to enhance consumer protection and create uniform supplement regulations across the EU (275).

1.5.4 Supplement Use: Prevalence

Dietary and herbal/botanical supplement use is highly prevalent among cancer survivors, with estimates ranging from 30% to 85% depending on population and region (276,277). In the United States, analyses of NHANES data (1999–2016) indicate that 66% of cancer survivors reported dietary supplement use, with breast and uterine cancer survivors being the highest users (277). A separate US cohort of 1,271 breast cancer survivors reported 89.5% used vitamin/mineral supplements and 67.7% used natural products, with 46.5% of vitamin/mineral users and 26.7% of natural product users taking three or more concurrently (278). Supplement use was higher in those receiving endocrine therapy ($p < 0.001$) and in those with hormone-receptor positive cancers (278).

Internationally, prevalence varies: 66.5% of Korean breast cancer survivors reported dietary supplement use, with higher education associated with use ($p = 0.02$) (167); 68.3% of French breast cancer survivors reported supplement use, with 18% using supplements contraindicated secondary to potential adverse effects (279); and 61% of Australian cancer survivors reported supplement use, with a median of two products per person (280). Oestrogenic botanical supplement use is particularly notable in breast cancer survivors, with 39.5% using at least one product and 21.1%

taking two or more concurrently (281). Use of these products was higher among younger, peri-menopausal women ($p < 0.001$) and those with higher education (281). In the UK, the DietCompLyf study observed 1,560 breast cancer patients, reporting dietary supplement use significantly increased one year post diagnosis ($p = 0.001$; 56.15% vs 62.8%) (282). Concerningly, oestrogenic botanical supplement use more than doubled following diagnosis ($p < 0.005$) with 56 types identified (282).

Overall, supplement use is consistently associated with female sex, higher education, younger or peri-menopausal status, and concurrent endocrine therapy (278,281,283,284). Motivations include perceived benefits for immunity, recurrence prevention, symptom management, and overall well-being. However, concerns exist regarding potential interactions with ongoing cancer therapies, inappropriate dosing, and lack of standardised clinical guidance (279,285). While the prevalence of dietary supplement use in cancer survivors is well-documented understanding the underlying motivations for such use is essential to contextualise these patterns and inform targeted health interventions, education and resources.

1.5.5 Supplement Use: Motivators

Marian (2017) noted that consumers are drawn to supplements, particularly botanicals, as they are natural, and therefore considered safe to assist in symptom management and improving quality of life (276). To note, there is no association with improvement in overall survival in cancer patients who use a dietary/botanical supplement compared to those who do not (277).

Common reasons cited for dietary and herbal supplement use include improving or maintaining overall health and wellbeing (279,284,286–290); prevent health problems or disease (286,289,290); manage adverse effects of anti-cancer therapies

(279,284,285,287,291,292); improve appearance or performance (279,287); something survivors can do for themselves (293); boost immune system (288–291,293); improve quality of life or coping mechanism (288,291); or improve the efficacy of systemic anti-cancer treatments (285).

Sarradon-Eck et al. (2020) observed that the use of non-conventional medicines, including dietary/herbal supplementation is a complementary means of coping with impaired health, such as a cancer diagnosis and the late effects of its treatment (287). The authors further highlighted that their use should alert physicians to potentially impaired quality of life (287).

However, this may pose a challenge, as historically cancer survivors do not typically disclose supplement use to their healthcare providers (276). In five international studies between 21.6% and 46.1% did not consult or disclose their supplement use to their healthcare provider, citing that the physician did not ask or they felt that the physician did not need to know (286,294,295,310,311). Contrastingly, three US and European studies reported between 51.1% and 82.4% disclosed supplement use to their healthcare provider (290,291,293). Concerningly, in a small cohort of US breast cancer survivors Silver, Goldenberg and Moore (2022) reported that 0% had an accurate list of dietary/herbal supplements documented in electronic medical records (295).

Dietary supplement use is highly prevalent in cancer survivors, with most using it to manage the late, long-term effects of treatment and improve overall wellbeing. In addition to understanding the reasons cancer survivors choose to use dietary supplements it is equally important to examine the sources of information that influence these decisions, as they can significantly shape perceptions of efficacy and

safety. Furthermore, it is pertinent to examine the nutritional considerations specific to people affected by early-stage breast and gynaecologic cancers, particularly in light of physiological, metabolic and nutritional changes associated with treatment-induced menopause, symptoms management and the postmenopausal period.

1.6 DIETETIC INTERVENTIONS IN CANCER SURVIVORS

Building on high supplement use and interest in MedD-type patterns, dietetic interventions offer a structured alternative for optimising survivorship nutrition. This section outlines dietetic interventions in breast and gynaecologic cancer survivors.

Dietetic interventions for cancer survivors are highly accepted and feasible across a range of modalities, as summarised in Table 1.8. These include group education, self-guided interventions, individualised counselling, and digital or remotely delivered programmes (240,296–328).

Multidisciplinary approaches combining dietetic interventions with physiotherapy or psychological support are also feasible and effective (Table 1.8). A variety of dietary patterns have been examined, including the WCRI/AICR dietary quality score, Mediterranean Diet, DASH diet, low-calorie diets, and adherence to American Cancer Society Guidelines, primarily in breast and endometrial cancer survivors with overweight or obesity (Table 1.8). Although a range of outcomes have been assessed across survivorship interventions, the majority of studies have historically prioritised weight loss or weight maintenance as primary endpoints, with comparatively less emphasis on body composition, functional outcomes, or patient-reported symptom burden.

1.6.1 Body Composition Measures Assessed in Dietetic Interventions for Survivors

Across studies, anthropometric and body composition outcomes were frequently evaluated. Core measures included body weight and BMI (240,297,298,300–302,306–308,312,313,316,319,321,323,324,329–336), waist or hip circumference (240,298,301,306,308,319,324,336), with weight loss, weight regain, and long-term weight trajectories often serving as primary endpoints. Several trials incorporated more detailed assessments of body composition, including fat mass, fat-free mass, lean body mass, visceral fat, and muscle mass, commonly measured via bioimpedance (306–308,312) or dual x-ray absorptiometry (DEXA) (298,301,302,319,324,330,331)

1.6.2 Dietary Assessments Used in Dietetic Interventions for Survivors

Dietary assessment was central across interventions using a range of validated tools such as 24-hour dietary recalls (ASA24, NDSR), 3-day records, food frequency questionnaires (FFQs), and 30-day dietary surveys (240,298,301,302,306,307,312,316,319,324,329–332). Diet quality was commonly quantified using established indices, including the Healthy Eating Index (HEI-2010) (302,306,316,323,337), Alternative Healthy Eating Index (AHEI-2010) (309), Dietary Quality Index (DQI, DQI-R) (296), and Rate Your Plate (310). Several studies specifically assessed adherence to dietary patterns such as the Mediterranean diet (240,308,312,332) or plant-based diets (311), while others focused on fruit and vegetable intake (298,299,313,323), percentage of dietary fat or macronutrients (315,324,329), or calcium intake from supplements or food (296,321).

1.6.3 Physical Activity Assessments used in Dietetic Interventions for Cancer Survivors

Physical activity outcomes were assessed through both self-reported and objective measures. Validated questionnaires such as the Godin-Shephard Leisure-Time Activity Questionnaire (299,313,323), the Stanford 7-Day Recall (298,312), and the

International Physical Activity Questionnaire (306,311) were widely used, while pedometer step counts (316,329) and accelerometer-based methods (e.g., ActivPal) (302,315) provided objective data. Some studies evaluated specific activity thresholds such as achieving moderate activity levels ≥4 METs (296,308). Fitness-based outcomes were less frequent but included standardised assessments such as the 3-minute step test (240), cycle ergometer performance (332), and handgrip strength (321).

1.6.4 Patient Reported Outcomes used in Dietetic Interventions for Cancer Survivors

Patient-reported outcomes (PROs) are central to many interventions, encompassing quality of life (QoL), psychological wellbeing, and behavioural self-efficacy. Quality of life is commonly measured using validated instruments such as the 36-Item Short Form Health Survey (SF-36), the Functional Assessment of Cancer Therapy-General (FACT-G), the Functional Assessment of Cancer Therapy-Breast (FACT-B), the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30), and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Breast Cancer Module 23 (EORTC QLQ-BR23) and related subscales (240,297,298,300–302,306,307,312,316,319,324,329–332).

Mental health outcomes, including depression, anxiety, and stress, are assessed using instruments such as the Beck Depression Inventory-Second Edition, the Centre for Epidemiologic Studies Depression Scale, the 2-Item Patient Health Questionnaire, the 4-Item Patient Health Questionnaire, the Beck Anxiety Inventory, the Hospital Anxiety and Depression Scale, and the Perceived Stress Scale (240,297,301,312,316,319,331). Other psychosocial domains evaluated include fear

of cancer recurrence, cancer worry, eating behaviours, body image, fatigue (measured with single-item visual analog scales or validated fatigue inventories), self-efficacy (for example, using the Weight Efficacy Lifestyle questionnaire), and social support or relational functioning (240,298,301,312,316,319,331,332,336).

Table 1.8 : Dietary Interventions in Breast and Gynaecologic Cancer Survivors

Author, Year	Cancer Type	Study Design	Sample Size / Population	Intervention Type	Dietary Focus	Use of ePROs	Outcome Measures	Key Findings
Gnagnarella et al. 2024 (324)	Breast	RCT (4 arm parallel)	266 women (BMI ≥ 25 kg/m^2)	Dietary Intervention (DI), Physical Activity Intervention (PAI), Physical Activity and Dietary Intervention (PADI), Minimal Intervention (MI)	Personalised dietary counselling using the World Cancer Research Fund recommendations ± physical activity over a 24 month period	Not specified	Body weight, fat mass, fat free mass, circumferences, glucose, triglycerides	DI: -3.8 kg (-4.3%); PADI: -3.1 kg (-3.6%). Significant fat mass reduction with FFM preserved; improvements in glucose and triglycerides; effects sustained at 12 and 24 months.
Skouroliakou et al. 2018 (308)	Breast	RCT (2 arm parallel)	70 women	Personalised dietary intervention or control group	Personalised dietary intervention based on the Mediterranean Diet or updated American Cancer Society dietary guidelines	No	Anthropometric and biochemical parameters, serum vitamin C, vitamin A, a-tocopherol and CoQ10 levels, dietary intake and adherence to MD	Significant reductions in body weight, BMI, waist circumference, and body fat, with increased HDL-C and vitamin C ($p < 0.002$); α-tocopherol increased, while CoQ10 was not significant after correction.
Parekh et al. 2018 (307)	Breast	RCT (2 arm parallel)	59 women	Six two-hour nutrition education workshops or nutrition brochures (control)	Dietitian-led workshops using WCRF/AICR recommendations	No	Feasibility, nutrition literacy (NLit-BCa), health literacy, food intake, height, and weight	High retention (89% control; 77% intervention). At 3 months, NLit-BCa effect sizes ranged from -0.5 to 0.16. Intervention deemed acceptable, with reported social and emotional support benefits.
Jen et al. 2004 (329)	Breast	RCT (4 arm parallel)	48 women (BMI >30kg/m^2)	Control, Weight Watchers, Individualised Counselling and Comprehensive Group	Behavioural weight-loss intervention (education, commercial programme, dietitian-led, or combined support)	No	Fasting blood sample, and three day dietary records	Weight loss: Control 1.1 kg; WW -2.7 kg; Individualised -8.0 kg; Comprehensive -9.5 kg. Only Individualised and Comprehensive reduced body fat; Comprehensive had greatest cholesterol and leptin improvements.

Author, Year	Cancer Type	Study Design	Sample Size / Population	Intervention Type	Dietary Focus	Use of ePROs	Outcome Measures	Key Findings
Reeves et al. 2021 (319)	Breast	RCT (2 arm parallel)	159 women (BMI 25 – 45kg/m^2)	12 month dietary intervention or usual care	Remotely delivered weight loss intervention including physical activity.	No	Weight, body composition, metabolic risk markers; Quality of life, fatigue, musculoskeletal and menopausal symptoms, body image, fear of recurrence	At 12 months, intervention participants improved vs usual care: weight -4.5%, fat mass -3.3 kg, metabolic syndrome risk -0.19, waist -3.2 cm, fasting glucose -0.23 mmol/L; physical QoL +2.7, musculoskeletal pain -0.5, body image -0.2 (all $p < 0.05$).
Befort et al. 2017 (301)	Breast	Second phase of RCT (2 arm parallel)	172 women who had lost ≥ 5% of baseline body weight from Phase 1	Phone based counselling or mailed newsletters	Calorie-restricted diet with up to 2 meal replacements/day	No	Weight regain over 12 months and measures of weight change and cost	Mean 6-month weight loss 14.0%; group phone participants regained less weight at follow-up (3.3 kg) vs newsletter (4.9 kg, $p = 0.03$). At 18 months, 75% of phone group maintained ≥5% weight loss vs 58% in newsletter ($p = 0.02$). Incremental cost-effectiveness: $882 per additional participant.
Lisevick et al. 2021 (330)	Breast	RCT (3 arm parallel)	100 women (BMI ≥ 25.0 kg/m^2)	Dietary intervention (in person or telephone based) or control	Calorie-restricted, plant-based lifestyle intervention with structured dietetic support	No	Primary: weight change up to 8 years post-intervention; Exploratory: associations between initial weight change (loss, maintenance, gain) and long-term weight trajectories	Over 8 years (mean 5.9 ± 1.9), both groups maintained initial weight loss (-6% intervention, -2% usual care) and continued modest decline (-0.20 kg/year, $p = 0.004$; -0.32 kg/year, $p = 0.002$), with no significant difference between groups ($p = 0.31$).
Sanft et al. 2018 (331)	Breast	RCT (3 arm parallel)	151 women (BMI ≥ 25.0 kg/m^2)	Dietary intervention (in person or telephone based) or control	Calorie-restricted lifestyle programme (diet + physical activity) with structured dietetic support	No	Anthropometrics (height, weight), blood markers (fasting), diet, physical activity, and relative telomere length	Among 125 participants, weight loss group showed 3% telomere lengthening vs 5% shortening in usual care ($p = 0.12$). In stage 0/I breast cancer, intervention led to 7% lengthening vs 8% shortening in control ($p = 0.01$); no effect in stage II/III.

Author, Year	Cancer Type	Study Design	Sample Size / Population	Intervention Type	Dietary Focus	Use of ePROs	Outcome Measures	Key Findings
Montagnese et al. 2020 (312)	Breast	RCT (2 arm parallel)	227 women	Mediterranean Diet + vitamin D supplementation ± physical activity	Traditional Mediterranean diet, low glycaemic index variant	No	Anthropometrics, diet (including Mediterranean diet adherence), biochemical markers, and HRQoL	Low-GI Mediterranean diet + brisk walking + vitamin D improved HRQoL, physical and social functioning ($p \leq 0.003$ - <0.001) and reduced fatigue and treatment-related symptoms ($p \leq 0.049$); benefits partly driven by BMI reduction and vitamin D sufficiency.
Chrisifano et al. 2016 (302)	Breast	Single arm prospective trial	180 women (BMI 27 – 45kg/m^2)	Group phone-based multidisciplinary lifestyle intervention	Calorie-restricted diet with meal replacements and lifestyle support	No	Demographics and treatment characteristics; Anthropometrics (weight, height, BMI); Dietary intake and quality assessed via 24-hour recalls and Healthy Eating Index 2010 (total and component scores)	Participants improved diet quality ($p = 0.001$) and lost 13.2% of body weight ($p = 0.001$); improvements in HEI and overall diet quality were associated with weight loss (HEI $p = 0.003$; diet quality $p = 0.01$).
Parma et al. 2022 (332)	Breast	RCT (2 arm parallel)	153 women (BMI ≥ 25.0 kg/m^2)	Multidisciplinary diet and lifestyle programme with workshops, motivational interviewing, and tailored newsletters. Usual care: informational brochures and non-MI calls	Anti-inflammatory (Mediterranean Diet)	No	Demographics and cancer characteristics; Psychosocial outcomes including depression, self-efficacy, cancer worry, perceived stress, and quality of life (FACT-G, FACT-B, CES-D)	Intervention improved perceived stress (PSS total score; $F(1,385) = 5.49$, $p = 0.019$); no significant effects on QoL measures or subscales, and no time or time × group interactions.
Zamorano et al. 2021 (335)	Endometrial	RCT (2 arm parallel)	80 women (BMI ≥ 30.0 kg/m^2)	Personalised text messaged weight loss intervention versus enhanced usual care	Healthy eating, physical activity, and behaviour self-monitoring programme	Not specified	Primary: Weight loss at 6 months. Secondary: weight loss at 12 months, body composition, quality of life, body image, physical activity, and comparison of clinical characteristics between participants and non-participants	Weight changes were similar between intervention and control at 6 months ($P = 0.08$); no differences in QoL, physical activity, or body image. Comparable proportions gained weight (~47%) or lost ≥5% (~10%) ($P = 0.85$).
Haggerty et al. 2019 (336)	Endometrial	RCT (3 arm parallel)	196 women (BMI ≥ 30.0 kg/m^2)	Telemedicine group versus text message group versus enhanced usual care	Calorie-restricted diet with lifestyle self-monitoring and physical activity targets	Not specified	Primary: Anthropometrics (weight, waist circumference, body composition) at 6 months;	Mean weight loss across interventions: -4.4 kg, no significant differences.

Author, Year	Cancer Type	Study Design	Sample Size / Population	Intervention Type	Dietary Focus	Use of ePROs	Outcome Measures	Key Findings
							Secondary: psychosocial outcomes including mood, quality of life, physical activity, sexual/relationship functioning, and body image	Telemedicine improved physical health and body image vs texting ($p = 0.04$) and sexual functioning vs EUC ($p = 0.03$); EUC increased total/vigorous PA vs telemedicine and texting ($p \leq 0.03$); texting increased walking vs telemedicine ($p = 0.02$).
Sheng et al. 2022 (333)	Breast	RCT (2 arm parallel)	94 women (BMI ≥25 kg/m^2, weight ≤400 pounds)	Multidisciplinary remote lifestyle intervention with telephone coaching and online self-monitoring versus control	Calorie-controlled diet with structured behaviour-change support	Yes	Primary: Physical function (PF) change at 6 months by weight-loss category (≥5% vs <5%); Secondary: proportion achieving minimally important change (5 points); Exploratory: other patient-reported outcomes by weight loss and study arm at 6 and 12 months	Participants achieving ≥5% weight loss had greater improvements in physical functioning at 6 (4.4 vs 0.3; $p = 0.02$) and 12 months (3.6 vs 0; $p = 0.04$). Non-significant improvements were seen for endocrine symptoms, fatigue, anxiety, and pain; no changes in sexual function, depression, or sleep.
Brown et al. 2022 (317)	Multiple (Breast 76.7%)	RCT (2 arm)	60 participants (BMI >25.0 kg/m^2)	Multidisciplinary group lifestyle intervention (diet + physical activity + behaviour support) versus wait list control	Calorie-restricted diet with structured behavioural weight-loss support	No	Anthropometrics (weight, BMI); Physical activity (accelerometer); Diet (intake via FFQ); Health-related quality of life including fatigue, sleep, and body image; Demographics and clinical characteristics	Over 15 weeks, the weight-loss program improved physical functioning (+6.2; $p = 0.02$), reduced insomnia (-17.1; $p = 0.03$) and sleep disturbance (-4.9; $p = 0.005$) vs waitlist. From week 15–30, prior participants maintained weight (+0.6 kg) while waitlist participants lost weight (-3.4 kg; $p < 0.001$).
Brown et al. 2021 (316)	Breast	RCT (4 arm)	351 women (BMI 25–50 kg/m^2)	Diet versus Exercise versus Diet and Exercise versus Control	Structured weight-loss diet with behavioural support and phased meal replacements	No	Health-related quality of life (SF-36; physical and mental health composites, subscales); Anthropometrics/arm volume; Demographics and	At 52 weeks, combined exercise + diet improved physical health summary score (ETD 5.39; 95% CI 0.55 to 10.22) and subscales (physical functioning, role-physical, vitality).

Author, Year	Cancer Type	Study Design	Sample Size / Population	Intervention Type	Dietary Focus	Use of ePROs	Outcome Measures	Key Findings
							clinical characteristics; Adverse events	Diet alone improved vitality (ETD 3.25; 95% CI -1.41 to 7.91). Exercise alone and all groups showed no change in mental health.
Raji Lahiji et al. 2022 (321)	Breast	RCT (2 arm, parallel)	90 women (scored ≥ 14 on Beck's depression test)	Nutritional counselling plus logotherapy versus nutritional counselling alone	Nutrition-focused intervention based on BCS dietary guidelines, with mood-boosting strategies	No	Psychological status (anxiety, depression, binge eating); Health-related quality of life; Anthropometrics (weight, BMI, waist, body fat, visceral fat, muscle mass, height); Dietary intake (energy, macro- and micronutrients from 3-day recalls)	Nutrition + logotherapy improved diet (fibre $p < 0.001$; vitamin C $p = 0.04$; other nutrients $p < 0.001$–0.002), reduced depression and anxiety (both $p < 0.001$), and enhanced global and multiple QoL domains ($p \leq 0.01$). Anthropometric changes occurred in both groups but were not significantly different.
Lee et al. 2014 (299)	Breast	RCT (2 arm, parallel)	59 women	Web-based self-management versus educational booklet (control)	Individually tailored diet and exercise program based on stage of change and ACS/WHO guidelines	Not specified	Primary: Physical activity (weekly moderate exercise), fruit & vegetable intake, diet quality (DQI); Secondary: Health-related quality of life, anxiety/depression, fatigue, stage of change, and self-efficacy for exercise and diet	At 12 weeks, the intervention improved exercise (≥150 min/week; $p < 0.0001$), fruit & vegetable intake (≥5 servings/day; $p = 0.001$), overall diet quality ($p = 0.001$), and protein/calcium adequacy ($p \leq 0.016$). Physical functioning and appetite improved ($p \leq 0.034$), fatigue decreased ($p = 0.032$), and exercise/F&V stage of change and self-efficacy increased ($p \leq 0.029$).
Braun et al. 2018 (306)	Multiple (Breast 59%)	Non-randomisded phase 2 trial	29 participants	Multi-component programme: urban garden harvesting, group education with cooking	Fruit- and vegetable-focused nutrition intervention with lifestyle self-monitoring	Not specified	Surveys: Quality of life and self-efficacy; Diet: intake and quality (30-day FFQ, HEI-2010); Physical activity: pedometer steps,	At 6 months, tele-MI improved weight (-4.8 kg vs -2.6 kg), waist, BP (-10.8 mm Hg; $p = 0.04$), cholesterol ($p \leq 0.02$), HRQoL (total, fatigue, sleep,

Author, Year	Cancer Type	Study Design	Sample Size / Population	Intervention Type	Dietary Focus	Use of ePROs	Outcome Measures	Key Findings
				demos, and weekly tele-MI versus non users			weight, goals (10,000 steps/day or 150 min/week); Clinical: weight, BMI, waist circumference, blood pressure, cholesterol, and plasma/skin carotenoids	fear, spirituality; $p \leq 0.05$), and diet quality (HEI; $p = 0.02$); steps/day increased non-significantly.
McCarroll et al. 2014 (300)	Endometrial	RCT (2 arm, parallel)	75 women (overweight or obese BMI)	Multidisciplinary lifestyle counselling versus usual care	Healthy diet with behavioural strategies targeting lifestyle change	No	Self-efficacy (WEL, 5 domains); Quality of life (FACT-G: physical, social/family, emotional, functional well-being)	SUCCEED improved all WEL domains and total score vs usual care; each 1-unit BMI decrease was associated with a 4.49-point WEL increase ($R = -0.356$; $p = 0.006$). FACT-G favoured SUCCEED for fatigue at 3 months ($p = 0.008$) and physical well-being at 6 months ($p = 0.048$); other domains were unchanged.
Miller et al. 2020 (311)	Multiple (Breast 58%)	RCT (2 arm, parallel)	54 participants	Multidisciplinary practical dietary intervention versus printed materials on plant-based diet	Cancer survivorship nutrition programme emphasising plant-based foods and healthy meal planning	No	Primary: Plant-based diet knowledge, confidence, and skills; Secondary: dietary intake (NCI Screener), quality of life (FACT-G7), psychological distress (PHQ-4), fatigue, emotional support (SOC8), and perceived barriers to fruits, vegetables, and whole grains	At weeks 9 and 15, the programme improved plant-based diet knowledge ($p < 0.05$), confidence, skills, and reduced barriers to fruit/vegetable intake; processed meat intake decreased. Other dietary and psychosocial changes were modest, with positive trends in plant-based intake and quality of life.

Author, Year	Cancer Type	Study Design	Sample Size / Population	Intervention Type	Dietary Focus	Use of ePROs	Outcome Measures	Key Findings
Koutoukidis et al. 2019 (309)	Endometrial	RCT (2 arm, parallel)	54 women	Group lifestyle programme with dietitian-led behavioural counselling versus control (booklet)	Healthy eating and lifestyle behaviour programme focusing on balanced diet, portion control, and physical activity	No	Diet (ASA 24-hour recall, AHEI-2010); Physical activity (Stanford 7-Day Recall, accelerometer subsample); Anthropometrics (weight, body composition, handgrip strength, blood pressure); Health-related quality of life (EORTC QLQ-C30/EN24); Healthcare resource use	At 8 weeks, the intervention improved diet (AHEI-2010 difference 7.5; 95% CI 0.1 to 14.9; p = 0.046) but not physical activity or global QoL. By 24 weeks, global QoL improved (difference 8.9; 95% CI 0.9 to 16.8; p = 0.029). Adherence was 77%, with no adverse events.
Vafa et al. 2020 (315)	Breast	RCT (3 arm, parallel)	121 women (BMI 25 – 35kg/m^2, with stage I-II lymphedema)	Calorie restricted diet + 10^9 CFU symbiotic supplement versus placebo versus control group	Individually prescribed calorie-restricted diet with or without synbiotic supplementation	No	Primary: Quality of life (LLIS: physical, psychosocial, functional); Secondary: Edema volume, BMI, diet (3-day 24-h recalls), and physical activity (IPAQ, MET-min/week)	At 10 weeks, CRS improved total QoL (p = 0.004), psychosocial (p = 0.022) and functional domains (p = 0.002), oedema volume (p = 0.002), and BMI (p < 0.001) versus control. No significant differences were seen between CRS and CRP.
Santa-Maria et al. 2020 (313)	Breast	RCT (2 arm, parallel)	87 women (BMI ≥25 kg/m^2)	Behavioural weight loss programme with telephone coaching and web/smartphone self-monitoring versus self-direct approach (control)	DASH-style reduced-calorie diet emphasising fruits and vegetables.	Not specified	Primary: Anthropometrics (weight, height, waist circumference, BMI); Secondary: Adipocytokines and inflammatory markers, metabolic panel (insulin, glucose, hs-CRP, lipids), and telomere length	At 6 and 12 months, 51% of POWER-remote participants lost ≥5% of baseline weight versus 12% - 17% in self-directed (OR = 7.9; 95% CI 2.6 to 23.9; p ≤ 0.003). Weight loss was linked to reduced leptin and improved inflammatory and lipid profiles.

Author, Year	Cancer Type	Study Design	Sample Size / Population	Intervention Type	Dietary Focus	Use of ePROs	Outcome Measures	Key Findings
Gray et al. 2019 (338)	Breast (45%), Prostate or Colorectal	RCT	487 participants	12-month tailored behavioural programme with mailed materials, telephone prompts, and counselling calls in urban versus rural	Tailored diet targeting high fruit/vegetable intake, low saturated fat, and modest weight loss	No	Primary: Physical function (SF-36 subscale and overall physical/mental component scores); Secondary: Physical activity (CHAMPS) and dietary intake (two 24-h recalls via NDSR)	Rural survivors showed slightly better physical functioning (+0.14 vs -0.74) and fewer adverse events (1.58 vs 1.64) than urban participants, but smaller improvements in fruit/vegetable intake (+1.47 vs +1.56; p = 0.018) and lower adherence to exercise and dietary goals.
Ruiz-Vozmediano et al. 2020 (240)	Breast	RCT (2 arm, parallel)	75 women	Dietary, exercise and mindfulness programme versus control	Mediterranean-style healthy eating with cancer prevention focus	No	Quality of life (EORTC QLQ-C30); Diet (FFQ, 24-hour recall, Mediterranean diet adherence); Anthropometrics (weight, height); Fasting blood markers (glucose, lipids, CEA, CA 15.3, full blood count)	At 6 months, the intervention improved physical and role functioning ($p \leq 0.028$), Mediterranean diet adherence ($p = 0.02$), and reduced BMI and weight ($p \leq 0.05$) versus control; dyspnoea increased slightly in the control group ($p = 0.066$)
Travier et al. 2013 (298)	Breast	Single Arm, Pre-Post	42 women (BMI ≥25 ≥ 40 kg/m^2)	12-week hospital-based programme combining diet and physical activity sessions, with pedometer support	Reduced-calorie diet (1,200 - 1,500 kcal/day) with healthy food choices and meal planning	No	Primary: Anthropometrics (weight, BMI, waist/hip, lean/fat mass), cardiorespiratory fitness (cycle ergometer), and physical activity (MET-hours/week from validated questionnaires); Secondary: Diet (FFQ, 3×24-h recalls) and quality of life (EORTC QLQ-C30, SF-36)	Participants attended >90% of sessions and lost 5.6 ± 2.0 kg, with reductions in BMI, fat mass, and waist circumference. Energy and nutrient intake decreased (energy -25%, fat -35%, saturated fat -37%, carbs -21%), while quality of life and cardiorespiratory fitness improved, supporting feasibility and effectiveness.
Demark-Wahnefried et al. 2015 (334)	Breast	RCT (2 arm, parallel)	692 women (BMI: 25 - 45 kg/m^2)	12-month intensive programme with weekly/tapering group sessions, personalised telephone/email guidance, and tailored quarterly newsletters versus control	ACS guideline-based healthy diet and physical activity programme	No	Anthropometrics (weight), Fitness (3-min step test), Physical activity (modified Godin); Surveys: Quality of life (SF-36, IOCv2, BCPT Symptom Scales) and depressive symptoms (CES-	At 6 months, the intervention maintained physical function (-3.45; 95% CI -6.10 to -0.79; $p = 0.011$) and limited symptom increases (0.10; 95% CI 0.04 to 0.16; $p = 0.002$) versus control;

Author, Year	Cancer Type	Study Design	Sample Size / Population	Intervention Type	Dietary Focus	Use of ePROs	Outcome Measures	Key Findings
							D), collected every 6 months for 2 years	vitality trended higher (p = 0.051). By 24 months, depressive symptoms increased slightly (-1.64; 95% CI -3.13 to -0.15; p = 0.031).
von Gruenigen et al. 2009 (297)	Endometrial	RCT (2 arm, parallel)	45 women (BMI: overweight or obese)	6-month multidisciplinary counselling programme delivered by dietitian, psychologist, and PI, including weekly-to-monthly sessions and additional remote contact versus control	Nutrition-focused lifestyle programme with behavioural support for diet, exercise, and weight management	No	Anthropometrics (weight, BMI, waist circumference); Quality of life (FACT-G, SF-36); Self-efficacy (WEL); Depression (BDI); Eating behavior (TFEQ), assessed at baseline, 3, 6, and 12 months	The lifestyle intervention improved self-efficacy for social pressure (p = 0.03) and dietary restraint (p = 0.02). Women who lost weight showed greater improvements in emotional well-being (p = 0.02), self-efficacy for negative emotions (p < 0.01), food availability (p = 0.03), physical discomfort (p = 0.01), and dietary restraint (p < 0.01) compared with those who gained weight.
Little et al. 2025 (339)	Breast (52.2%), Prostate or Colorectal	RCT (3 arm, parallel)	2712 participants	Generic support versus complex digital lifestyle intervention ± additional support via email and telephone	Diet, weight management, and physical activity with symptom and distress management	Yes	Primary: Quality of life (EORTC QLQ-C30 summary score); Secondary: EORTC QLQ-C30 subscales, depression, anxiety, fear of recurrence, MYCaW QoL, enablement, healthcare resource use, and website engagement/adherence	At 6 months, all groups improved QLQ-C30 scores; by 12 months, Renewed with support showed small additional global health gains (1.42; 95% CI 0.33 to 2.51) and improvements in symptoms and enablement, with reduced primary care costs. No harms reported.

Author, Year	Cancer Type	Study Design	Sample Size / Population	Intervention Type	Dietary Focus	Use of ePROs	Outcome Measures	Key Findings
Synder et al. 2007 (296)	Breast or Prostate	RCT (2 arm, parallel)	182 participants	6-month programme with 12 telephone counselling sessions and personalised workbook, guided by Transtheoretical and Social Cognitive Theory versus general health workbook (control)	Personalised diet targeting fat, saturated fat, cholesterol, fruits, vegetables, whole grains, calcium, and iron based on national guidelines	No	Dietary intake (3 unannounced 24-h recalls); Food grouped by Food Guide Pyramid including supplement calcium; Overall diet quality (DQI-R, 0-100 points, nutrient and food-based components)	At 6 months, the intervention improved overall diet quality (67.6 to 69.8) and dietary diversity (4.8 to 4.8) versus declines in controls (67.5 to 64.6 and 4.7 to 4.1; $p \leq 0.003$).
Cairo et al. 2020 (310)	Breast	RCT (2 arm, parallel)	127 women	Personalised smartphone-based coaching via Vida app, including diet, exercise, sleep, and weight tracking with video, phone, and messaging support versus self-guided toolkit with printed resources, exercise band, pedometer, and walking DVD (control)	Healthy diet, exercise, and weight management with self-monitoring and lifestyle coaching	No	Physical activity (Godin-Shephard Leisure-Time Questionnaire); Diet quality (Rate Your Plate); Fatigue (single-item VAS); Depression (PHQ-2); Follow-up at 12 months: app/toolkit use, weight, adherence, and intervention feedback	At 6 months, the app group achieved greater weight loss and BMI reduction ($p < 0.01$), increased strenuous physical activity ($p = 0.04$), and improved dietary patterns ($p < 0.001$) versus the self-guided group. Fatigue and depression improved non-significantly. At 12 months, app use ceased, though many maintained wellness plans and weight loss; low response rates limited evaluation.
Lopez-Pentecost et al. 2023 (322)	Multiple (Breast 67%)	Mixed methods pilot intervention	13 cancer survivors + 6 care givers (Hispanic ethnicity)	Two-week text-message programme (26 intervention + 26 polling messages) using COM-B framework, with personalised coaching support	ACS guideline-based nutrition and physical activity delivered via culturally tailored, low-burden behaviour-change messages	No	Feasibility (recruitment, retention, response rates ≥80%); Acceptability (polling texts, exit interviews); Qualitative feedback on satisfaction, content, behaviour change, and cultural relevance	The text-message intervention was feasible, well-accepted, and cost-effective. Physical activity texts were rated more acceptable by survivors (94%) than nutrition texts (86%), while caregivers rated both equally (91%), supporting potential for promoting lifestyle changes in Hispanic cancer survivors and caregivers.
Puklin et al. 2023 (323)	Breast	RCT	205 women (BMI ≥25 kg/m^2)	26-week self-guided programme with book, website, instructional	Increased fruit and vegetable intake, reduced energy intake (1200-	No	Primary: Body weight (self-reported at baseline, 6, and 12 months);	At 6 months, the intervention achieved greater weight loss

Author, Year	Cancer Type	Study Design	Sample Size / Population	Intervention Type	Dietary Focus	Use of ePROs	Outcome Measures	Key Findings
				videos, pedometer use, weekly self-weighing, and behaviour-change strategies (goal setting, self-monitoring) based on Social Cognitive Theory versus waitlist control	2000 kcal/day), higher fibre, limited fat (<25% of total energy), and physical activity (150 min/week + 10,000 steps/day)		Secondary: Physical activity (questionnaires: type, intensity, minutes/week), Diet (120-item FFQ, HEI-2010, components: fruits, vegetables, fibre, % fat), Quality of life (FACT-G, FACT-B, FACT-ES, FACIT-F)	than waitlist (-1.3 kg; 95% CI -2.5 to -0.13). Improvements in physical activity (+18.7 min/week), diet quality (HEI +3.2), and fatigue (FACIT-F +1.4) were observed but not statistically significant.
Suzuki et al. 2020 (314)	Breast	Single arm prospective study	32 women	Multidisciplinary 3-week programme including dietitian-led nutrition education, health coach-led behavioural sessions, supervised group aerobic exercise, and optional at-home exercise video	Healthy eating guidance with self-monitoring of meals and weight, combined with aerobic exercise and behavioural education	No	Anthropometrics (weight, BMI, arm circumference, skinfolds); Biochemical markers (liver enzymes, cholesterol, triglycerides); Psychosocial measures (distress: K6, fatigue: CFS, self-efficacy: SES); Participant feedback on group intervention, assessed at baseline, 1, 3, and 6 months	Participants showed significant improvements at 1 month in body weight, BMI, triglycerides, total cholesterol, psychological distress, and cancer-related fatigue (all $p < 0.05$). At 3 and 6 months, further reductions were observed in body weight, BMI, and triceps skinfold thickness ($p < 0.05$).
Trejo et al. 2024 (327)	Breast	Single arm interventional study	17 women	Five weekly 2-hour group medical visits with a multidisciplinary team (navigator, oncologist, nurse, dietitian, psychologist, sexual health counsellor) covering survivorship care, symptom management, and lifestyle guidance	Healthy diet and lifestyle guidance as part of comprehensive survivorship care, including symptom management, emotional and sexual health support	No	Participant experience (pre/post surveys, NCCN distress thermometer, debriefing interviews); Feasibility (recruitment >70%, delivery >80%, survey completion >70%, sample representativeness); Acceptability (completion rates >70%, post-survey feedback, interviews)	High engagement and completion rates (76-100%). Post-intervention, participants reported increased familiarity with survivorship care plans (67% vs 22%), confidence in recognising long-term side effects (67% vs 28%), and awareness of supportive programmes (67% vs 33%; all $p \leq 0.01$). Sessions on primary care/oncology, sexual health, and emotional health were rated highly useful.

Abbreviations: AHEI, Alternative Healthy Eating Index; AICR, American Institute for Cancer Research; ACS, American Cancer Society; APP, Advanced Practice Provider; BAI, Beck Anxiety Inventory; BCPT, Breast Cancer Prevention Trial (Symptom Scales); BDI-II, Beck Depression Inventory II; BFI-K, Brief Fatigue Inventory (Korean version); BRAS, Breast Cancer Anxiety Subscale [FACT-B]; BRBI, Breast Cancer Role-Physical Subscale [FACT-B]; BRBS, Breast Cancer Role-Social Subscale [FACT-B]; BRFU, Breast Cancer Follow-Up [FACT-B]; BRHL, Breast Cancer Health Literacy; BRSEE, Breast Cancer Emotional/Exercise Engagement; BRSEF, Breast Cancer Social/Emotional Function; BRST, Breast Cancer Specific Task (subscale); CCK, Cooking for Cancer Kitchen programme; CI, Confidence Interval; COM-B, Capability, Opportunity, Motivation – Behaviour model; CoQ10, Coenzyme Q10; CRF, Cardiorespiratory Fitness; CRP, Calorie-Restricted diet + Placebo; CRS, Calorie-Restricted diet + Synbiotic; CTCAE, Common Terminology Criteria for Adverse Events; DASH, Dietary Approaches to Stop Hypertension; DI, Dietary Intervention; DQI, Diet Quality Index; DQI-R, Diet Quality Index – Revised; EORTC QLQ-BR23, Breast Cancer-Specific Module; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; ePRO, electronic Patient-Reported Outcome; EQ-5D-3L, EuroQol-5 Dimensions, 3 Levels; EUC, Enhanced Usual Care; F&V, Fruits and Vegetables; FACIT, Functional Assessment of Chronic Illness Therapy; FACT, Functional Assessment of Cancer Therapy; FFM, Fat-Free Mass; FFQ, Food Frequency Questionnaire; FM, Fat Mass; GMV, Group Medical Visit; HDL-C, High-Density Lipoprotein Cholesterol; HEI, Healthy Eating Index; HRQoL, Health-Related Quality of Life; IOCv2, Impact of Cancer version 2; iOTA, Interactive Obesity Treatment Approach; IPAQ, International Physical Activity Questionnaire; LEAN, Lifestyle, Exercise, and Nutrition program; LLIS, Lymphedema Life Impact Scale; MBSR, Mindfulness-Based Stress Reduction; MD, Medical Doctor; MET, Metabolic Equivalent Task; MI, Minimal Intervention; MI (in Parma et al.), Motivational Interviewing; MOS, Medical Outcomes Study; MVPA, Moderate-to-Vigorous Physical Activity; NCI, National Cancer Institute; NCCN, National Comprehensive Cancer Network; NLit-BCa, Nutrition Literacy Tool for Breast Cancer; PADI, Physical Activity and Dietary Intervention; PAI, Physical Activity Intervention; PF, Physical Function; PHQ, Patient Health Questionnaire; PHQ-4, Patient Health Questionnaire-4; POWER, Preventing Obesity With Education & Resources; PRO, Patient-Reported Outcome; PROMIS, Patient-Reported Outcomes Measurement Information System; PSS, Perceived Stress Scale; qPCR, quantitative Polymerase Chain Reaction; RCT, Randomised Controlled Trial; RD, Registered Dietitian; RENEW, Reach out to ENhancE Wellness; RTL, Relative Telomere Length; SD, Standard Deviation; SF-36, Short Form Health Survey (36-item); SOC8, Sense of Community scale, 8-item); TFEQ, Three-Factor Eating Questionnaire; TTM, Transtheoretical Model; WCRF, World Cancer Research Fund; WEL, Weight Efficacy Lifestyle Questionnaire; WHO, World Health Organisation; WSEDI, Web-Based Self-Directed Intervention

1.6.5 Feasibility Assessments used in Dietetic Survivorship Interventions

Several studies incorporated feasibility and process evaluations. Recruitment, retention, and completion rates were commonly reported with thresholds often applied as indicators of feasibility (240,297,298,300–302,306,307,312,316,319,324,329–332,336). Acceptability was explored through participant feedback, text message responses, exit surveys, and qualitative interviews, which were thematically analysed for satisfaction, cultural relevance, and perceived behaviour change (240,297,298,301,302,312,316,319,324,330,331). Intervention adherence was captured through dietary compliance, physical activity monitoring, or digital engagement metrics, while some studies included cost-effectiveness analyses (240,297,298,300–302,306,307,312,316,319,324,329–332,336).

1.6.6 Clinical and Treatment Related Outcomes Assessed in Dietetic Survivorship Interventions

Studies collected clinical and treatment-related outcomes to contextualise lifestyle changes in cancer survivors (Table 1.8). These included participant demographics, treatment characteristics, physical symptoms such as musculoskeletal pain and menopausal or treatment-related side effects (240,297,298,300–302,306,307,312,316,319,324,329,330,332) and healthcare resource use in some trials (306,324,331).

Biochemical and molecular outcomes assessed metabolic health and disease risk, including fasting glucose, insulin, triglycerides, cholesterol, C-reactive protein, adipocytokines, inflammatory markers, liver enzymes, and antioxidant status (vitamin C, vitamin A, alpha-tocopherol, Coenzyme Q10) (240,306,312,316,319,324,331,332). Molecular markers such as telomere length and

tumour biomarkers, including carcinoembryonic antigen and cancer antigen 15.3, as well as composite indices such as the metabolic syndrome risk score, were also reported in some cohorts (240,306,312,319,331).

1.6.7 Effects of Dietetic and Lifestyle Interventions in Cancer Survivors

Dietetic and lifestyle interventions in breast and gynaecologic cancer survivors predominantly report modest but consistent improvements in weight, BMI, and fat mass, with fewer studies assessing broader outcomes such as muscle mass, functional status, or symptom burden. For example, Gnagnarella et al. (2024) reported weight loss of -3.8 kg (diet-only) and -3.1 kg (diet plus physical activity), with sustained improvements in glucose and triglycerides at 12 and 24 months (324), while Skouroliakou et al. (2018) observed reductions of -2.25 kg and -2.88 kg, respectively (308). Interventions were generally well-tolerated, with high retention (329)

Multicomponent and individualised programmes achieve greater outcomes than standard approaches. Reeves et al. (2021) found only individualised comprehensive programmes significantly reduced fat mass and improved cholesterol and leptin (319). Befort et al. (2016) reported reductions in metabolic syndrome risk score, waist circumference, and fasting glucose, alongside improved physical quality of life and body image (301). Long-term maintenance is variable: Lisevick et al. (2021) observed higher 18-month weight-loss maintenance with phone-based groups (330), while Sanft et al. (2018) found diminished between-group differences at eight years (331).

Evidence on cancer-specific and molecular endpoints is limited. Montagnese et al. (2020) reported telomere lengthening in early-stage breast cancer survivors (312).

Low-glycaemic Mediterranean diets and vitamin D supplementation improved HRQoL, fatigue, and therapy-related symptoms (302). Psychosocial outcomes are variable, often linked to achieving ≥5% weight loss (336).

Digital interventions are feasible and acceptable, improving weight, diet quality, physical activity, and selected HRQoL domains, though long-term engagement often declines (316,317).

In summary, dietetic and lifestyle interventions provide short- to medium-term benefits for weight, metabolic health, and select quality-of-life outcomes. Critical gaps remain in long-term maintenance, cancer-specific outcomes, psychosocial effects, and tailored interventions for gynaecologic cancer survivors.

1.7 ELECTRONIC PATIENT REPORTED OUTCOMES

While dietetic interventions demonstrate feasibility, their real-world impact depends on identifying patients with actionable nutrition-related symptoms. Patient-reported outcomes help bridge this gap, as they capture a patient's health status directly from the patient, without interpretation by clinicians or any other individual (340).

Enhanced collection of patient-reported outcomes (PROs) and health-related quality of life (HRQOL) data is essential. PROs provide valuable insights into health status and can guide clinical decision-making. Increasingly, electronic data collection methods are being adopted, allowing for remote, real-time monitoring and improving communication between patients and healthcare providers. In a 2014 review, thirty-three unique systems implemented in cancer clinical practice were identified, with nineteen systems used as patient-centred systems following patients across treatment and survivorship periods (341). The review highlighted that patient-centred systems were likely to be integrated into large electronic hospital records, provide more

robust scoring options and importantly, more likely to provide user-friendly features for service users (341).

More recently, a 2024 umbrella review (n = 222 unique studies) highlighted key oncology care interventions utilising patient-reported outcome measures (PROMs), including symptom monitoring, feedback-driven clinical decision-making, and integration into multidisciplinary care pathways (342). From a dietetics perspective, these findings are particularly relevant, as PROMs provide actionable insights into nutrition-related symptoms such as menopausal symptoms, gastrointestinal disturbances, weight fluctuations, and fatigue, all of which directly impact dietary intake, nutritional status, and overall survivorship outcomes. The evidence demonstrates that PROM feedback improves symptom control, enhances patient-provider communication, and increases adherence to supportive care interventions, ultimately contributing to better quality of life and clinical outcomes for cancer survivors (342). Electronic PROMs (ePROs) have demonstrated high completion rates and feasibility in breast and gynaecologic cancer populations (343–345) supporting timely identification of nutrition and psychosocial needs. Both patients and healthcare professionals report greater satisfaction when PROMs address relevant symptoms and are integrated into consultations, allowing immediate responses to adverse scores (346).

Embedding dietitians within multidisciplinary teams (MDTs) that utilise ePROs enhances access to supportive care, including nutrition and symptom management, ultimately improving survivorship outcomes. Challenges remain in integrating ePROs with electronic health records, limiting large-scale data analytics (347). Future integration of ePRO platforms could further empower dietitians and the MDT to

deliver precision nutrition and symptom management, advancing survivorship care for breast and gynaecologic cancer patients.

1.8 CURRENT DIETETIC SPHERE IN IRELAND

Research on dietetic and dietary interventions in cancer survivorship is expanding, but implementation in clinical practice remains limited. In Ireland, one dietitian serves approximately 4,500 oncology patients and a recent survey reported 45.5 whole-time equivalent dietitians across eight cancer centres and a paediatric unit, most based in the capital city (Dublin), and managing mixed caseloads (348).

Between 2020 and 2022, there were 24,207 invasive cancers were diagnosed annually (2), meaning the ratio of dietitians to newly diagnosed patients is roughly 1 to 532, excluding those already under care. While dietitians are included in multidisciplinary teams in most cancer centres, participation outside these centres is much lower (348). Irish cancer survivors indicate a strong preference for live online nutrition talks (26.8%) and identify dietitians as their primary source of reliable information (320), with print and digital resources providing additional autonomy to access evidence-based guidance at their own pace (349). Furthermore, nutrition misinformation remains a significant concern, with 56% of survivors reporting confusion from online sources (350).

Dietitians play a specialised and multifaceted role in supporting hormone receptor positive breast cancer and gynaecologic cancer survivors (Figure 1.2), yet the scarcity of large-scale trials and dedicated posts in Ireland continues to limit the translation of research into clinical care.

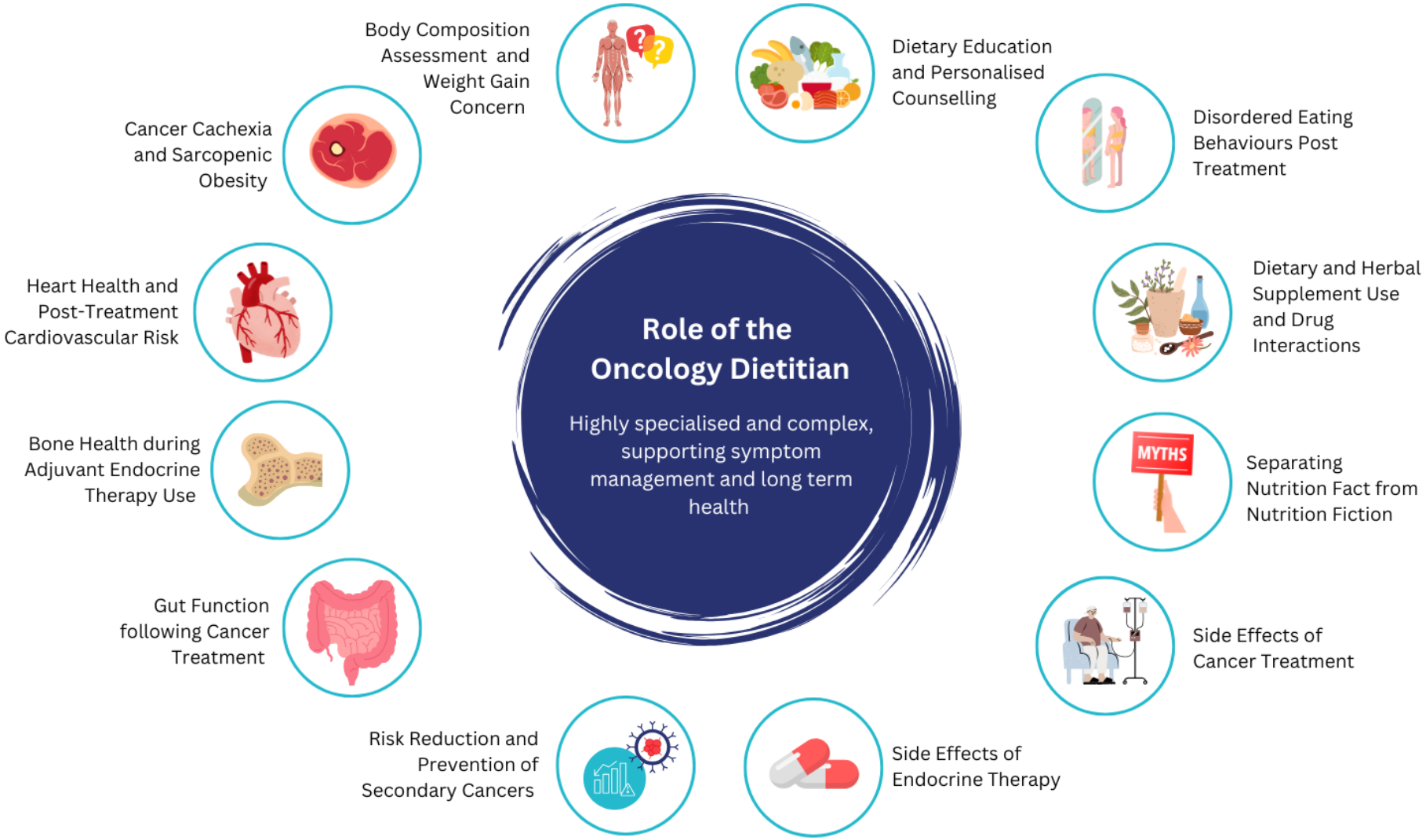


Figure 1.2: Role of the Oncology Dietitian in Cancer Survivorship Care

1.9 CONCLUSION

This chapter has critically examined the existing evidence on the nutritional needs of breast and gynaecologic cancer survivors with the aim of understanding the implementation of targeted dietetic interventions in a cohort of early-stage hormone-receptor positive breast and gynaecologic cancer survivors who may be impacted by iatrogenic menopause.

This review underscores the effectiveness of a multi-disciplinary approach in improving survivorship outcomes, particularly in weight-based interventions. However, most studies remain limited in scope, focusing on weight management rather than broader measures such as quality of life, adherence to dietary quality scores, symptom management or patient reported concerns, factors that significantly impact long-term survivorship.

Current dietetic practice predominantly relies on traditional methods, such as low-calories diets and face-to-face counselling, but these approaches often lack practical adaptation to the evolving healthcare landscape. For example, electronic patient reported outcomes for remote monitoring, efficient use of clinical time and maximising healthcare resources remain underutilised. This reflects a broader tension between the traditional role of the dietitian, centred on weight management, and their complex skill set, which could address symptom management and proactive dietary strategies.

Significant gaps remain in the literature, including the proactive nature of interventions, lack of symptom-focused resources, limited understanding of longitudinal supplement use, and insufficient exploration of reasons for disclosures of supplement use to healthcare professionals. Methodological gaps, such as the absence

of tailored, ready-made, patient-specific resources and validated digital tools further limit progress. Addressing these gaps offers the potential to develop the first dedicated dietetic survivorship service and patient-specific resources that optimise both healthcare resource use and individual outcomes.

In summary, this review highlights the current state of knowledge on targeted dietetic interventions in early-stage breast and gynaecologic cancer survivors, identifies critical gaps, and established the foundation for subsequent investigation. By addressing the unique intersection of cancer survivorship, iatrogenic menopause and nutritional needs, the following studies seek to advance understanding and practice in this critical area of support.

1.10 AIMS AND OBJECTIVES OF THESIS

The aims and objectives of this thesis are as follows:

(1) to assess the feasibility of a dietitian- and nurse-led survivorship clinic in two regional cancer centres using electronic patient reported outcomes in early-stage breast and gynaecologic cancer survivors;

(2) to evaluate the impact of a dietitian-led intervention in meeting the nutrition-specific needs of breast and gynaecologic cancer survivors and to investigate their influence on body composition, dietary quality and supplement use;

(3) to investigate the prevalence, information source and perceived effectiveness of dietary and herbal supplements in female cancer survivors impacted by iatrogenic menopause;

(4) to contribute to the development and dissemination of evidenced-based resources and strategies with a primary focus on the integral role of dietitians in cancer survivorship.

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CHAPTER 2: A DIETITIAN SURVIVORSHIP CLINIC FOR EARLY-STAGE BREAST AND GYNAECOLOGIC CANCER SURVIVORS: A DIETETIC PROTOCOL FOR THE LINKING YOU TO SUPPORT AND ADVICE (LYSA) RANDOMISED CONTROLLED TRIAL

This work has been published in HRB Open Research:

Johnston KE, O'Connell K, McSharry V et al. *A Dietitian Survivorship Clinic for Early-Stage Breast and Gynaecologic Cancer Survivors: A Dietetic Protocol for the Linking You to Support and Advice (LYSA) Randomised Controlled Trial [version 1; peer review: awaiting peer review]. HRB Open Res 2025, **8**:77 (https://doi.org/10.12688/hrbopenres.14187.1)*

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2.1 ABSTRACT

Background: To align with the EU Beating Cancer Plan, feasible and innovative solutions that monitor specific needs of cancer survivors, improve quality of life and long-term disease-free survival need to be investigated. The Linking You to Support and Advice (LYSA) Trial was a multisite, randomised feasibility trial, co-designed with public and patient involvement. Eligible participants had early-stage hormone receptor (HR)-positive breast or gynaecologic cancer, completed primary curative treatment within 12 months and had internet access (NCT05035173). The 12-month intervention involved a dietitian- and nurse-led clinic targeting symptom management. Detailed protocols targeted towards dietetic services and interventions are limited in this cohort. The dietetic component of the LYSA Trial aimed to evaluate the impact of using electronic patient reported outcomes (ePROs) on diet quality and body composition in HR-positive breast and gynaecologic cancer survivors. Over 12 months, changes in dietary intake, nutritional risk, body weight, lean tissue mass, adipose tissue mass and muscle strength were assessed.

Methods: Comprehensive anthropometric and nutritional assessments were conducted at baseline and 12 months for both study arms. These included body composition through bioelectrical impedance analysis and World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) diet quality score. Participants in the experimental arm completed ePROs every 2 months for one year, assessing malnutrition risk, physical activity and weight gain concerns. A trigger-initiated nutritional management pathway, delivered via a telehealth platform, was developed for worsening or severe individualised symptoms.

Conclusion: This protocol outlines the implementation of a dietetic cancer survivorship clinic, within a randomised control trial. The use of ePROs and digital

technologies offers viable and innovative solutions to monitor the nutrition-specific needs of cancer survivors. Findings will inform the development of future dietetic survivorship services.

2.2 INTRODUCTION

Breast cancer is reported to make up 30% of all invasive cancer incidences in Ireland, with the 5-year observed survival being 78% (1). The 5-year observed survival in cervix cancer is 63% and uterus cancer is 71% (1). Advances in treatment and early detection have seen improvements in 5-year net survival, however this has also seen the insufficient, uncoordinated management of late and long-term effects of treatment (1,2). These effects encompass a wide range of symptoms, including physiological, psychological, cognitive, social, sexual, and nutritional challenges (3). They may be equal or more disabling than a cancer diagnosis and its treatment, and can significantly affect quality of life (4). Furthermore, an individual's transition from "active patient" to "survivor" is often challenging and associated with lifestyle and behavioural changes, including those related to diet and nutrition (5–7). In Ireland, cancer survivorship is regarded as a distinct and important phase of the cancer journey and a priority in the National Cancer Strategy (2017-2026), and it is broadly accepted that a cancer survivor is defined as a person "living with and beyond cancer", from the point of diagnosis and continuing until the end of life (8).

Chemotherapy receipt, menopausal status and adjuvant endocrine therapy are all proposed to be major contributors to alterations in body compositions throughout the cancer journey (7,9–14). Furthermore, these factors play a key role in the treatment of gynaecologic cancers (15,16). The use of an adjuvant endocrine therapy, such as a selective oestrogen receptor modulator (SERM) or an aromatase inhibitor (AI) can reduce the risk of breast cancer recurrence by 30% to 50% after 5 years of therapy and improve disease free survival (14,17). These adjuvant endocrine therapies are associated with side effects that impact quality of life, physical activity, sleep and

mood, as well as accelerating menopausal status and symptoms (4,18). Whilst the impact of chemotherapy and radiotherapy on body composition has been well documented, literature around the impact of adjuvant endocrine therapy is limited in comparison. Body composition alterations include decreasing lean tissue mass and increasing adipose tissue mass, with Aleixo et al. (2018) identifying sarcopenia and obesity as important risk factors for adjuvant endocrine therapy toxicity and intolerance (19). Furthermore, sarcopenia has been identified as an independent factor in disease-free-survival and overall survival (17). Weight gain after breast cancer is reported in up to 90% of patients (14). It is widely reported that breast cancer survivors, those with Grade 2 or 3 obesity (defined as Body Mass Index [BMI] >35kg/m^2) have a worse survival compared to those with normal weight. There are inconsistent conclusions for the association of Grade 1 obesity (defined as BMI > 25kg/m^2) with survival outcomes (19).

Changes in body composition and dietary quality in breast and gynaecologic cancer survivors are due to a myriad of complex factors including genetic predisposition, socio-demographic factors, menopausal status, hormone-receptor status, clinical presentation and treatment modality. There is well documented evidence that body composition parameters, including lean tissue mass and adipose tissue, are suggested to be predictors of survival. In light of this, the National Comprehensive Cancer Network's Survivorship Guidelines recommend that a multidisciplinary approach is used and that providers should be competent advising survivors how to achieve an optimal body composition, including low overall body fat and higher amounts of muscle mass (20). Adjuvant therapies, including endocrine therapies, have significantly improved survival rates in female cancers, but also lead to a range of

short- and long-term nutritional risks. These nutritional risks extend beyond those traditionally associated with cancer treatment, including increased risk of bone disease, cardiovascular disease, obesity and metabolic disturbances secondary to their treatment (21–24). These are further compounded by treatment induced menopause (25). The unique nutritional challenges faced by this cohort highlight the need for targeted dietetic care post-treatment to enhance long-term survival support chronic disease risk reduction and improve quality of life.

Despite this need, the implementation of high-quality dietetic outpatient survivorship care can be hindered by personnel shortages, access to the multidisciplinary team and travel barriers (26). A growing body of evidence supports the use of electronic and remote means as a supplement to usual care to aid the management of physical side effects, psychosocial effects, health promotion and disease prevention in post treatment care for cancer survivors (26). Digital solutions offer a promising approach to delivering holistic, patient-centred care, particularly in rural areas (27). Virtual consultations extend the reach of dietitians, reduce the burden of and need for in person visits, and enhance patient engagement. The use of patient reported outcomes (PROs) allows healthcare professionals to monitor specific symptoms in real time and provide intervention in an efficient and timely manner. Dietetic interventions for cancer survivors are highly accepted (5,28,29) and have been shown to be feasible across a range of delivery modalities (30–40). In particular, telephone consultations have shown to be feasible and effective in oncology weight management research (30,32,34,38).

Despite growing recognition of the acceptability and feasibility of dietetic care in the post-treatment phase, there are currently no dedicated dietetic survivorship services

embedded within the Irish healthcare system. This represents a critical gap, particularly given the well-documented nutritional challenges faced by cancer survivors, including changes in body composition, persistent treatment-related side effects, and increased risk of comorbidities. Although the LYSA Trial's protocol paper has been published, it provides only a high-level summary of the dietetic intervention, offering limited insight into the practicalities of its implementation or the rationale behind its design (41). The dietetic component of the LYSA intervention is both novel and complex, incorporating trigger-initiated follow-up, electronic patient-reported outcomes (ePROs), and a hybrid model of in-person and remote delivery. These elements reflect an innovative, patient-centred approach tailored to the real-world constraints of outpatient oncology care. Given the increasing emphasis on scalable and resource-efficient survivorship models, a dedicated protocol paper is warranted to describe the development, structure, and operationalisation of this intervention in detail.

2.3 AIMS AND OBJECTIVES

This chapter therefore aims to expand on the LYSA intervention and address this gap by outlining the design, delivery, and rationale of a dietetic survivorship clinic tailored for breast and gynaecologic cancer survivors in an Irish outpatient oncology setting. In doing so, it offers a replicable model for integrating structured nutritional care into cancer survivorship services, with potential relevance both nationally and internationally as healthcare systems seek to optimise post-treatment support.

2.4 MATERIALS AND METHODS

2.4.1 Study Design

The LYSA trial was a multi-centre randomised controlled trial (RCT) with an active comparator and experimental arm. LYSA assessed the feasibility of introducing a complex intervention incorporating a dietitian- and nurse-led cancer survivorship clinic, symptom management through ePROs (Figure 2.1). The trial was across medical oncology outpatient clinics in two regional cancer centres in Ireland.

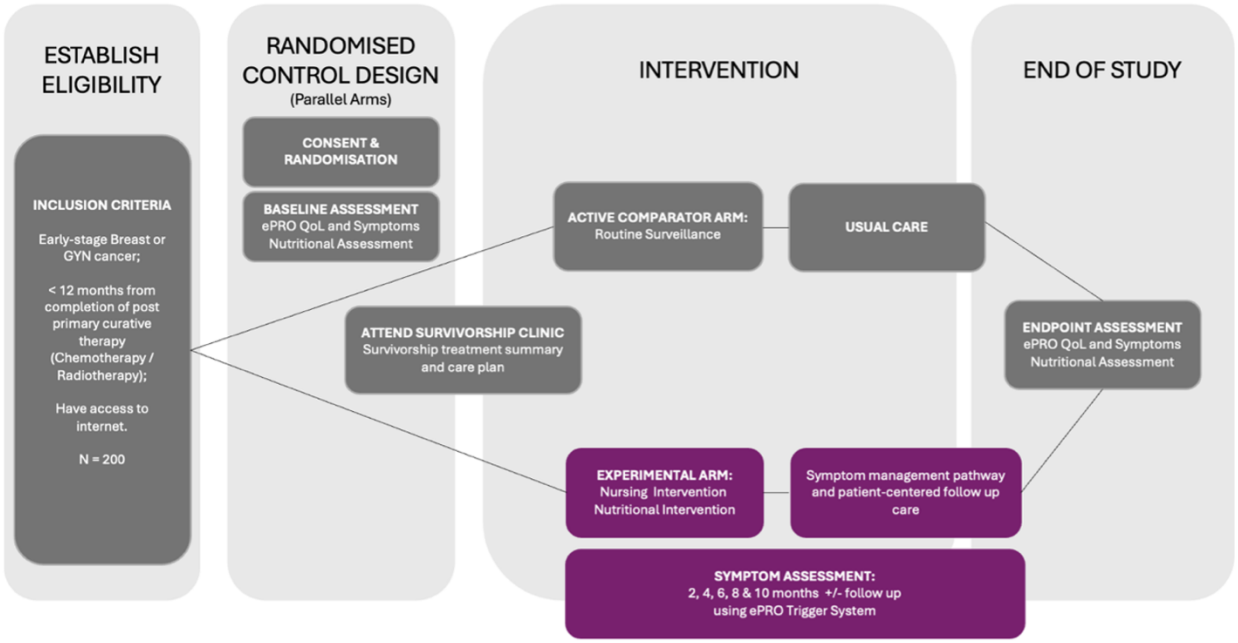


Figure 2.1. The LYSA Trial Study Design

2.4.2 LYSA Trial Dietetic Aims

The aim of the dietetic aspect of this survivorship clinic in HR-positive breast and gynaecologic cancer survivors enrolled in the LSYA Trial were to:

(1) Assess the feasibility of delivering a dietetic survivorship clinic supported by electronic patient-reported outcomes (ePROs) within an Irish medical

oncology outpatient setting, including the use of ePRO data to inform patient monitoring and guide dietetic review within the intervention pathway.

(2) Evaluate changes in dietary intake and diet quality over a 12-month period in the experimental arm compared to usual care.

(3) Evaluate changes in body composition and related outcomes including body weight, lean tissue mass, adipose tissue mass, muscle strength, nutritional risk and weight gain concern over a 12-month period in the experimental arm compared to usual care.

2.4.3 Research Ethics

The trial was conducted in accordance with the Declaration of Helsinki, the application sections of the International Council of Harmonisation (ICH) E6 Good Clinical Practices and the terms of approval of the responsible research ethics committee across two Irish cancer centres. The trial was registered with ClinicalTrials.gov [NCT05035173].

2.4.4 Eligibility Criteria

Detailed inclusion and exclusion criteria were outlined in the LYSA Primary Protocol (41). Participants were eligible for inclusion if they were aged ≥18 years; diagnosed with early-stage breast or gynaecologic cancer; and within 12 months of completing primary curative treatment. Breast cancer participants were required to have stage I - III hormone receptor-positive disease (oestrogen receptor and/or progesterone receptor ≥1%) and HER2-negative disease according to ASCO-CAP guidelines, or to be scheduled to commence adjuvant endocrine therapy during the study period. Gynaecologic cancer eligibility included cervical cancer (stage I-III) and endometrial cancer treated with curative intent, including adjuvant radiotherapy with or without

chemotherapy. Individuals with premalignant disease (e.g., ductal carcinoma in situ or lobular carcinoma in situ) were also eligible. Additional inclusion criteria included access to the internet, ability to provide written informed consent, and ability to read and understand English.

Participants were excluded if they had not been treated with curative intent, were unable in the judgement of the Principal Investigator or study team to engage with the protocol (including inability to attend hospital visits or communicate effectively in English), or had participated in a similar lifestyle or survivorship intervention within the previous 12 months.

2.4.5 Sample Size and Randomisation

The sample size was based on the recruitment of the largest possible sample given the numbers of potentially eligible patients during the time frame of the study and funding availability to facilitate the feasibility and pilot efficacy objectives: n = 200 (41). The study was not powered to detect treatment effects, and all secondary dietary and body composition outcomes were considered exploratory efficacy outcomes intended to inform future definitive trial design. Randomisation was conducted by the study's principal statistician via an electronic data capture platform, (Castor Electronic Data Capture [EDC]). Randomisation was stratified by cancer diagnosis in a 1:1 ratio for breast cancer, cervical cancer and endometrial cancer using a computer-generated randomisation list, and randomly sized blocks of size 4, 6, or 8. Research team members were not blinded to participants' group allocation due to the intervention's nature.

2.4.6 Data Management

The dietetic data for both arms was collected by the clinical research dietitians at two sites on approved case report forms (CRFs). All data were entered into Castor EDC, designed specifically for the LYSA trial. The Castor EDC met international guidelines with respect to data protection standards. The study data were assessed for incompatible, discrepant, or clinically implausible values. Any concerning data were reconciled against the original source data. Following the completion of data "cleaning", the Castor EDC Database was locked. The source data, including dietetic CRFs, was filed in the participants' medical notes as per hospital guidelines at the point of study completion.

2.4.7 Dietetic Intervention

The measurements tools used at baseline (T0) and 12-month (T12) survivorship clinics were the same for both arms as described in Table 2.1. The experimental arm was informed of their body composition and handgrip strength measurements as part of the intervention.

At or prior to the baseline (T0) clinic, the research nurse at each site sent the initial electronic survey to the participants' designated email addresses via Castor EDC. This electronic survey aimed to evaluate various factors including body weight (kg), height (cm), Malnutrition Screening Tool score (MST) (42), weight gain concern, and physical activity status, utilising the Nordic Physical Activity Questionnaire-short (43). Upon survey completion, they attended the LYSA Survivorship Clinic in an outpatient regional cancer centre. Consultations were guided by survey results.

Participants attended a combined survivorship clinic appointment comprising 60 minutes with a dietitian and 60 minutes with a nurse. Clinic capacity was structured

to accommodate a maximum of five participants per site per week across participating centres. Clinic lists included a mixture of participants attending at baseline (T0) and 12-month follow-up (T12), depending on their study timepoint within the intervention schedule.

Table 2.1: The LYSA Dietetic Survivorship Clinic Intervention Schedule

Experimental and Active Comparator Study Schedule	**Study Time Period (Months)**						
	T0	**T2**	**T4**	**T6**	**T8**	**T10**	**T12**
Online Diet Symptom Survey (ePRO) Weight Gain Concern, Physical Activity, MST Score and Body Weight (BMI)	AC E	E	E	E	E	E	AC E
Anthropometry: Weight, Height, Waist Circumference	AC E						AC E
Bioelectrical Impedance Analysis: Lean Tissue Mass, Adipose Tissue Mass, Lean Tissue Index, Fat Tissue Index	AC E						AC E
Muscle Strength: Hand Grip Strength	AC E						AC E
Dietary Intake: Multiple 24HR Dietary Recalls *(1 Person and 1 Virtual)* FFQ	AC E						AC E
Cancer-Specific Dietary Quality: WCRF/AICR Score	AC E						AC E
Body Weight Assessment	AC E						AC E
Cancer-Specific Diet Education	E						E
Personalised Nutritional Counselling (As Required)	E	E	E	E	E	E	AC E

Abbreviations: AC: Active Comparator; E: Experimental; ePRO: electronic patient reported outcome; 24HR: 24 hour; FFQ: Food Frequency Questionnaire; MST: Malnutrition Screening Tool; WCRF/AICR: World Cancer Research Fund/American Institute for Cancer Research

The dietitian completed the following anthropometric measurements and nutritional assessments during the baseline and 12-month outpatient appointments:

Body Mass Index: BMI was calculated by the participant's weight in kg to the nearest 0.1kg, using the SECA Model 799 weighing scales, and their height in metres to the 0.01m, using SECA 206 stadiometer.

Waist Circumference: Waist circumference was measured to the nearest 0.1cm following the WHO STEPS Manual (44). The measurement was conducted three times, and the mean value was used.

Body Composition: Body composition was measured via bioelectrical impedance analysis (BIA) using the Fresenius Kabi Body Composition Monitor (BCM, Fresenius Medical Care, Bad Homburg, Germany). Measurements included lean tissue mass, lean tissue index, adipose tissue mass, fat tissue index, total body water, body cell mass, extracellular water and intracellular water. Participants who had pacemakers, implanted electronic devices or were pregnant were excluded from this measurement. The quality value for each measurement aimed to be > 85. Although recent consensus guidelines recommend reporting fat-free mass (FFM) for BIA-derived measures, the terminology used in this thesis reflects the proprietary output variables provided by the BCM device (including lean tissue mass).

Handgrip Strength: Handgrip strength was measured using Jamar dynamometer *(Jamar Hydraulic Hand Dynamometer, Model 091011725, Sammons Preston Roylan, Nottinghamshire, UK)*, using the second handle position as recommended by the American Society of Hand Therapists. The measurement was taken three times on each hand, alternating each measurement to allow a break. The average of three measurements was taken.

Multiple 24-Hour Dietary Recall: Two 24-hour dietary recalls were conducted using a weekday and weekend-day to allow accurate energy intake (45).The multiple pass method was used to standardise the 24 hour recall (46). The dietary recall was entered by the research dietitian into Nutritics software (v6.00), for nutritional analysis.

Food Frequency Questionnaire: The EPIC NORFOLK FFQ was used (*version CAMB/PQ/6/1205*) to allow a comprehensive overview of each participants' dietary habits over the course of one year (47). The participant's completed the FFQ between their first baseline clinic visit and their follow up virtual clinic visit at T0 (Figure 2.2). Participants' verbally reported their FFQ answers to the dietitian, who then entered them into a FETA template for nutritional analysis. Following their 12-month visit, participants returned the FFQ by post using a stamped and labelled envelope provided by the research dietitian.

Diet Quality: Diet quality was assessed using the WCRF/AICR standardised scoring system. The score included eight of the ten Cancer Prevention Recommendations (48,49). The score specifically investigated BMI; waist circumference; physical activity status; intake of fruit, vegetables and fibre, percentage of total kilocalories from ultra-processed foods (UPFs), red and processed meat, sugar sweetened beverages and alcohol; and breast-feeding history (49,50). Each recommendation was scored as 1 (meeting recommendation), 0.5 (partially meeting recommendation) or 0 (not meeting recommendation) points (48–50).The scores ranged from 0 to 8 points, with higher scores reflecting greater adherence to recommendations. The dietitian calculated this score using anthropometric data, 24 hour recall dietary intake and food frequency questionnaire from baseline and 12 months. Scores from the UPF recommendation were calculated as tertiles, using the complete data set from 24 hour

dietary recalls at baseline and 12 months. Dietitians manually calculated the total percentage of kilocalories from UPF consumed using Nutritics software (v6.00).

2.4.7.1 Experimental Arm Intervention

Following the baseline anthropometric and nutritional assessments, the experimental arm received a written "Nutrition Pack" containing "*Healthy Eating For Cancer Survivors",* (51) a booklet containing the WCRF Recommendations and healthy recipes; the Health Service Executive (HSE) Weekly Low Risk Guidelines for Alcohol; Let's Get Active Leaflet; and two sample walking programmes. The information was verbally relayed to participants by the dietitian via a telehealth platform, which allowed for information to be described and adapted to fit the individuals' own circumstances. Following this education session, the experimental arm received personalised nutritional counselling following the Nutrition Care Process (52) and the behaviour change model (53) to ensure that dietetic care was standardised across both sites.

Following the Nutrition Care Process, Nutrition Assessment and Diagnosis was conducted at the baseline outpatient visit. At the baseline virtual visit (Figure 2.2), using the behavioural change model (53), motivational interviewing (54) and shared decision-making (55), the Nutrition Intervention was conducted. This determined the dietetic prescription, formulated achievable goals and directed action. Nutrition Monitoring and Evaluation was conducted using the trigger-initiated ePROs every two months. This was assessed through electronic surveys, received via email.

Experimental Arm Flow Through the "Linking You to Supports and Advice" LYSA Trial Dietetic Intervention

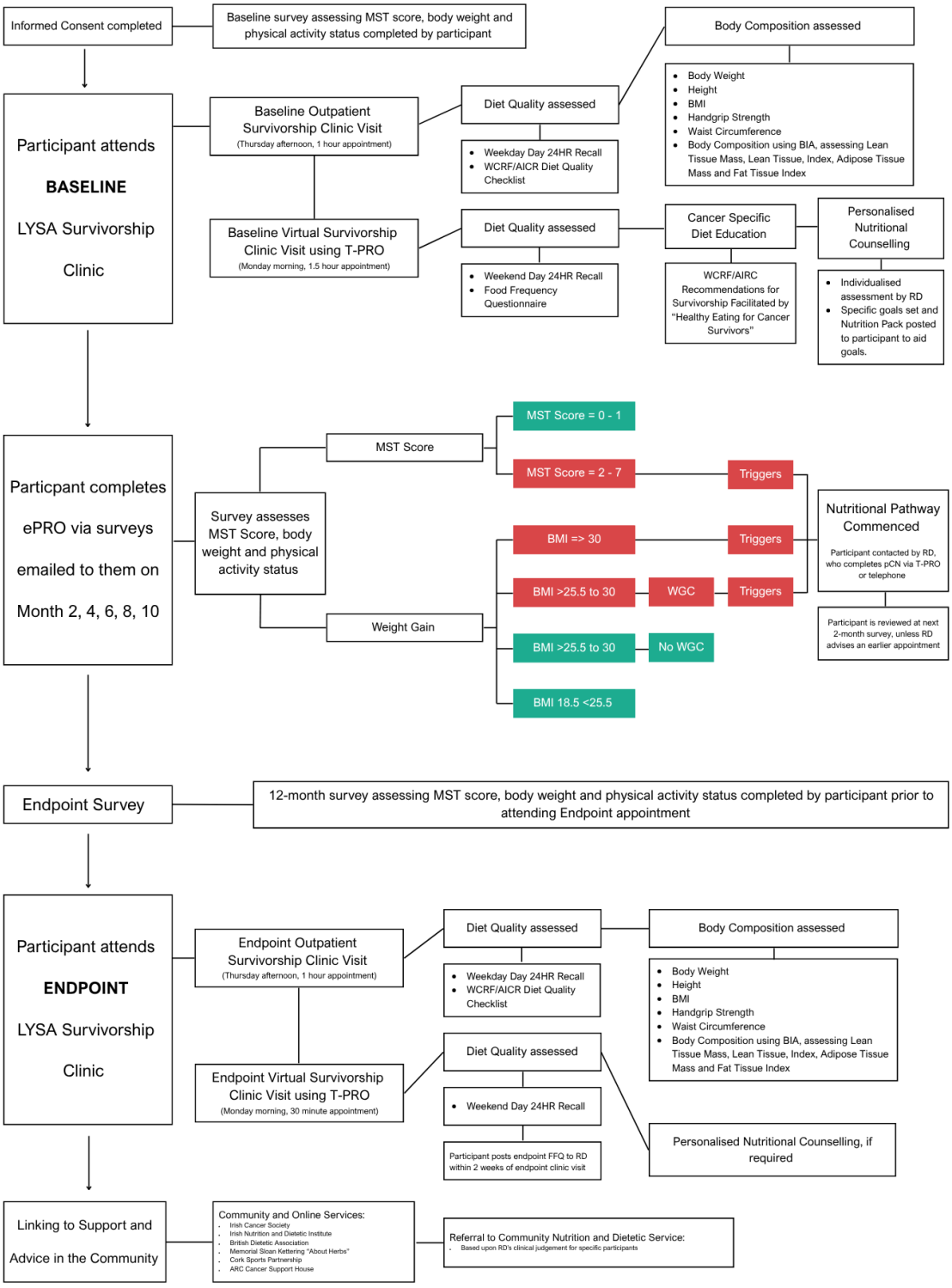


Figure 2.2. The Experimental Arm Flow through the LYSA Trial

Abbreviations: 24HR: 24-hour; BIA: Bioelectrical Impedance Analysis; BMI: Body Mass Index; FFQ: Food Frequency Questionnaire; LYSA: Linking You to Support and Advice; MST: Malnutrition Screening Tool; PCN: Personalised Nutritional Counselling; RD: Registered Dietitian; WCRF/AICR: World Cancer Research Fund/American Institute for Cancer Research; WGC: Weight Gain Concern

2.4.7.2 ePROs Trigger System

The ePROs collected at baseline and month 12 for both arms, and additionally at 2, 4, 6, 8, 10 for the experimental arm, were translated into a colour-coordinated trigger system. There was a maximum of two dietitians at each site conducting dietetic consultations using a standardised approach. Dietetic ePROs survey questions were broken into two sections: 1) diet and 2) exercise, with questions directly translating into the trigger scoring system (Table 2.2).

Table 2.2. Dietetic ePRO Survey Questions

Section	Question	Possible Answers	Linked Trigger:
Diet	1. Have you lost weight recently without trying?	Yes No Unsure	MST Score
	2. If yes, how much weight have you lost? (kg/lbs)	1-5kg (2-12lbs) 6-10kg (13-24lbs) 11-15kg (24-33lbs) >15kg (34lbs or more) Unsure	MST Score
	3. Have you been eating poorly because of a reduced appetite (eating less food at mealtimes, eating less often)?	Yes No	MST Score
	4. What is your weight today?	_____ kg	BMI
	5. Are you concerned about weight gain?	Yes No Unsure	WGC
Exercise	**Physical Activity** 1. In general, over the last month how many minutes per week have you spent walking?	_____ Total minutes per week	No trigger

Moderate-Vigorous Physical Activities 2. On a typical week, how much time do you spend in total on moderate and vigorous physical activity, where your heartbeat increases and you breathe faster? *Examples include: brisk walking, cycling as a means of transport or as exercise, heavy gardening, cleaning-heavy (washing windows, vacuuming, mopping) or recreational sports (badminton, tennis, dancing)?*	Only include activities that lasted at least 10 minutes at a time. Less than 75 minutes Between 75 minutes and less than 150 minutes More than 150 minutes	No trigger
Vigorous Physical Activities 3. How much of the time that you spend on physical activities in a typical week, which you indicated above, do you spend in total on vigorous physical activities? This includes activities that require hard physical effort, get your heart racing, make you sweat and breathe much harder than normal (e.g. swimming, hiking, jogging (at 6mph), running, bicycling fast (14-16mph), cardio training, weight-lifting, carrying heavy loads, shovelling or team sports such as basketball or soccer games, tennis).	Only include activities that lasted at least 10 minutes at a time. Less than 75 minutes Between 75 minutes and less than 150 minutes More than 150 minutes	No trigger

Abbreviations: BMI: Body Mass Index; kg: kilograms; lbs: pounds; MST: Malnutrition Screening Tool; WGC: Weight Gain Concern

Participants triggered a nutritional pathway if they had: an MST score of 2-7; BMI >30; or a BMI 25.5-30kg/m^2 and weight gain concern (Figure 2.2).

The research nurse used the R Project for Statistical Computing and the RStudio integrated development environment (IDE) statistical software packages to produce a

trigger list for research dietitians (Figure 2.3). If participants triggered, they were contacted by the research dietitian and a review was conducted using the telehealth platform T-Pro or via telephone consultation. Participants were contacted by the research dietitian up to three times within a week of the trigger. If participants did not make contact, they were classed as a "did not attend" (DNA) and were reviewed at the next survey.

The research dietitians had access to the nursing trigger list, which included symptoms such as fatigue, urinary urgency, constipation, diarrhoea, insomnia and fear of recurrence, to allow for a comprehensive dietetic assessment. Nutritional counselling was adapted to the specific trigger, and the subsequent dietetic assessment that was conducted. Overall, nutritional counselling focused on optimal body composition, including muscle mass and bone mineral density, regardless of body weight, through protein and calcium intake. Protein intake was targeted at 1.5g – 2.0g Protein per kilogram of body weight per day (kg/BW/d) (56) and standard nutrition support advice, as per the National Clinical Guideline 22 (57), was given to participants with an MST >2 and/or a BMI <18.5, including food fortification and the use of oral nutritional supplements when required. For participants with MST >2 and/or a BMI <18.5, a goal of 25kcal - 30kcal and 1.5g - 2.0g Protein per kilogram of body weight was set, as per ESPEN Guidelines (58).

For participants with BMI >=25.5kg/m^2 and WGC or BMI >30kg/m^2, behavioural change and motivational interviewing was incorporated as part of the care plan, as per the Irish Nutrition and Dietetic Institute (INDI) Position on Optimal Approaches to Adult Weight Management Services in Ireland (59). Stable dietary and meal patterns were established focusing on optimal protein intake and where appropriate, recommendations included up to a 600kcal daily energy deficit (59). SMART

(specific, measurable, achievable, relevant and timebound) goals were established at each consultation following a patient-led approach. At subsequent trigger-initiated consultations, these SMART goals were evaluated, with external triggers and antecedents to eating behaviours identified. In individual cases where clinical judgement dictated appropriate the dietitian could review before the next 2-month survey.

The experimental arm completed their endpoint survey at 12 months and were invited to attend the 12-month Survivorship Clinic. Participant results were compared from baseline and if clinically appropriate, a final personalised nutritional counselling session was conducted. For participants where clinical judgement dictated appropriate, a consented referral to the relevant Community Nutrition and Dietetic Service was made for nutrition support or weight management.

2.4.7.3 Active Comparator Arm

Following the baseline anthropometric and nutritional assessments, participants randomised to the active comparator arm underwent routine surveillance. They completed their endpoint survey at 12 months, assessing MST score, body weight, weight gain concern and physical activity status (Figure 2.3). The ePROs were translated into a colour-coordinated trigger system by the research nurse.

Upon completion of their 12-month survey, the active comparator arm was invited to attend the 12-month (T12) Outpatient Survivorship Clinic. Participants who had triggered at their 12-month survey were offered a personalised nutritional counselling session which was conducted at the point of study completion (Figure 2.3). They also received the same Nutrition Pack as the experimental arm, posted to them upon completion of the study. For active comparator arm participants where clinical

judgement dictated appropriate, a consented referral to the relevant Community Nutrition and Dietetic Service was made for nutrition support or weight management.

2.4.8 Adverse Events

The study was deemed low risk by the study sponsor based on the stated intervention. The process for adverse events is outlined in the Primary Protocol (41).

2.4.9 Statistical Analysis

The statistical analysis has been published the in the Primary Protocol (41). Data were processed and analysed using descriptive and inferential statistics using the R Studio Package. Preliminary analyses was carried out to ensure that the assumptions of normality, linearity or homoscedasticity are not violated. Means and standard deviations were presented for normally distributed data, while medians and interquartile ranges were used to describe non-parametric data. Chi Squared test or Fishers exact tests were used to compare categorical variables. Mann Whitney U tests were used to investigate differences in continuous, non-parametric data.

Participants' demographics and cancer characteristics, including menopausal status and adjuvant endocrine therapy use, were presented as descriptive statistics including mean (SD), median (range) and proportions.

A generalised linear mixed model test was performed to determine the mean differences in lean tissue mass, adipose tissue mass, body weight, handgrip strength, waist circumference and other health outcomes between women in the experimental arm and the active comparator arm over time and group by time interaction.

Active Comparator Arm Flow Through the "Linking You to Supports and Advice" LYSA Trial Dietetic Intervention

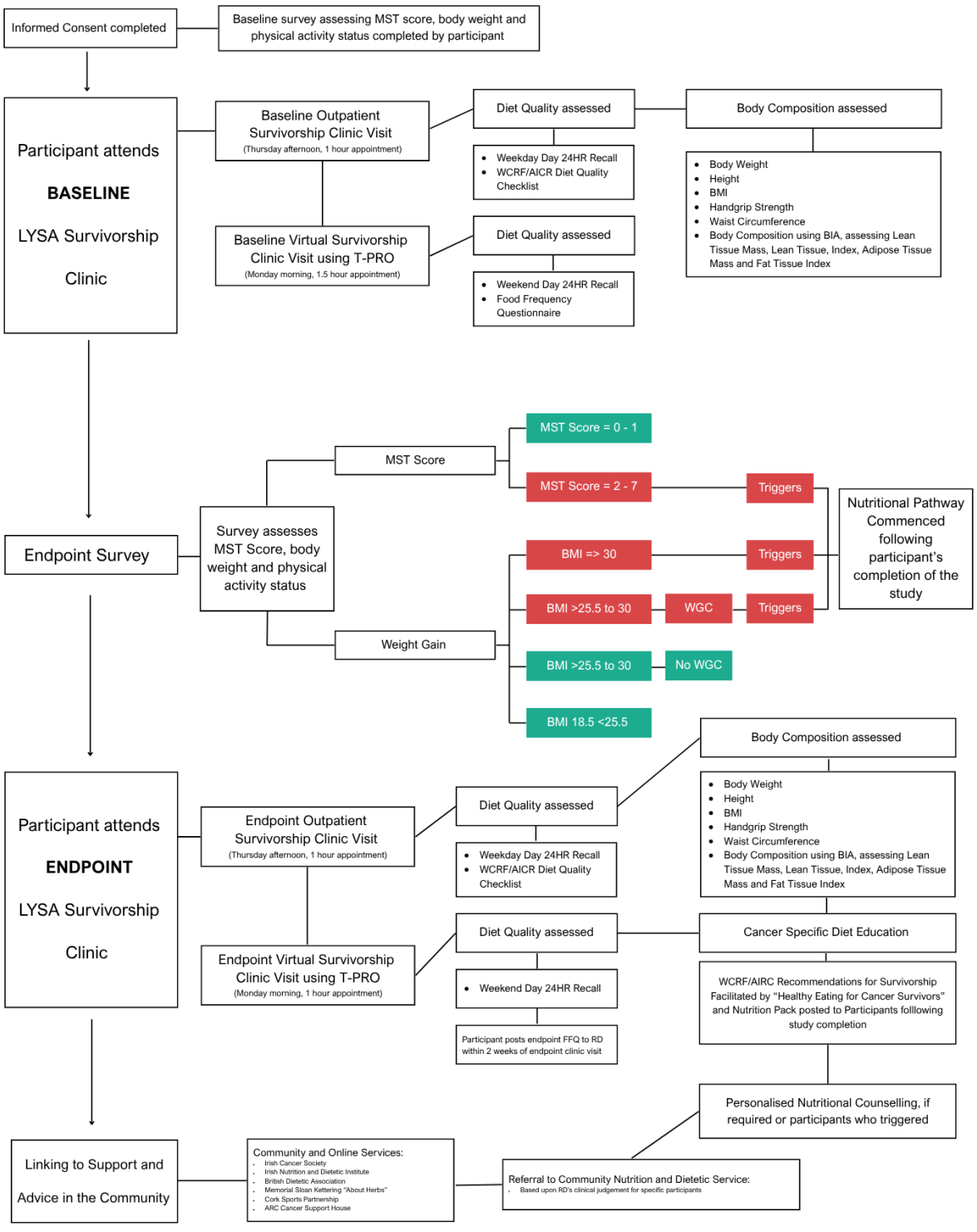


Figure 2.3. The Active Comparator Arm Flow through the LYSA Trial

24HR: 24-hour; BIA: Bioelectrical Impedance Analysis; BMI: Body Mass Index; FFQ: Food Frequency Questionnaire; LYSA: Linking You to Support and Advice; MST: Malnutrition Screening Tool; PCN: Personalised Nutritional Counselling; RD: Registered Dietitian; WCRF/AICR: World Cancer Research Fund/American Institute for Cancer Research; WGC: Weight Gain Concern

Nutritics was utilised to capture dietary intake information, and data from the multiple 24HR assessments were analysed using the UK's composition of foods data from McCance and Widdowson's integrated dataset (60), the United States Department of Agriculture (USDA) Food Composition Database (61), and the Irish food composition database (62). Data concerning changes in nutritional status were complemented by nutrient data from the European Prospective Investigation into Cancer Study EPIC-Norfolk Food Frequency Questionnaire (FFQ) (47) based on version 6 (CAMB/PQ/6/1205). Data gathered via the FFQ were entered into a validated processing tool, the FFQ EPIC Tool for Analysis (FETA), based on the Compositional Analyses from Frequency Estimates (CAFE) system (63). Changes in diet quality scores was based on the WCRF/AICR standardised scoring system (49,50), with higher scores representing a better diet quality.

2.4.10 Patient Involvement

The study team members collaborated with a public and patient involvement (PPI) panel in the design, development, implementation, analysis, and dissemination of the study. The PPI panel included patient advocates who have had breast or gynaecologic cancers, and stakeholders including clinical and academic experts, wider members of the multidisciplinary team and community support groups.

2.5 DISCUSSION

The primary aim of the Linking You to Support and Advice (LYSA) randomized controlled trial was to evaluate, for the first time, the feasibility of dietitian- and nurse-led survivorship clinics for early-stage breast and gynaecologic cancer survivors in Irish cancer centres, using electronic patient-reported outcomes (ePROs). The purpose

of this protocol paper was to describe the implementation of the dietetic intervention in detail to contribute to the growing body of literature around supportive care.

Meeting the nutrition-specific needs of this growing cohort of cancer survivors may prove a challenge in today's climate. Research globally has reported that access to a dietitian is a barrier: in breast and gynaecologic survivors, only 12%-34% reported engaging with a dietitian at least once post-treatment (28,29) but 35%-60% reported moderate to severe nutrition impact symptoms (29), perceived muscle loss, dietary problems and the desire to engage with a dietitian (28). The impact of body composition as a prognostic outcome has been well documented (56), but it is still not incorporated into routine care within the Irish setting. A greater effort should be in place to make body composition assessment accessible to all healthcare and medical professionals, not only through primary curative treatment but particularly following its completion, to monitor the impact and effect of the former.

Sarcopenia is common in breast and gynaecologic cancers, affecting 11%-67% of patients (64–70). It is now recognised to include muscle strength and performance, no longer solely characterised by low muscle mass (56). Low muscle mass has been associated with increased toxicity-related endocrine therapy discontinuation (*OR 2.18, $p = 0.036$*), subsequently worse ipsilateral breast tumour recurrence and disease-free survival (*HR 9.47, $p = 0.002$; HR 4.53, $p = 0.001$*) (14), and a 71% increased mortality risk in breast cancer survivors (66). Sarcopenic obesity, characterised by high adiposity and low muscle mass, further increases mortality and treatment complications, with BMI proving an unreliable prognostic factor (14,71). Chemotherapy contributes to metabolic syndrome in 73% of patients and increases inflammation by 32%, (21) while cancer treatments can also accelerate bone loss, with a 21% reduction in bone density within 6 months (21–24). Whilst chemotherapy and

endocrine therapy are associated with increased visceral adipose tissue (VAT) in breast cancer (68,69) research examining the effects of endocrine therapy on muscle mass in breast cancer has been variable, with one study showing an increase muscle mass (69) but others demonstrated a decrease in skeletal muscle index (72,73). Further long-term research is warranted to contribute to the understanding of endocrine therapies relationship with body composition. The LYSA Trial will provide the first Irish data set, comparing changes in muscle mass during the first years of endocrine therapy (active comparator arm) and the impact of dietary counselling (experimental arm) for a 12 month period.

Oncology dietitians, who have upskilled in the area of body composition analysis, are in the unique position to assess, diagnose, intervene and monitor important prognostic factors, such as muscle mass and adipose tissue mass. The impact of a body composition assessment should not be ignored, however in routine clinical assessment due to a myriad of factors, anthropometric measurements are limited to weight, height and BMI. The breast and gynaecologic cancer cohort may be particularly at risk of sarcopenic obesity due to the impact of menopausal status and adjuvant endocrine therapy as well as weight gain during systemic anti-cancer treatment. Given the inconsistencies of BMI as a prognosis factor in individuals with overweight or obesity in relation to DFS, assessment of body composition has evolved to be a more informative approach (19). This protocol details the use of practical and accessible techniques for assessing body composition in the outpatient setting, including handgrip strength (HGS), waist circumference (WC), and bioelectrical impedance analysis (BIA). These methods are not only feasible for routine clinical use by dietitians in acute and outpatient settings but also hold promise as valid indicators of nutritional and functional status. While each has known limitations - such as HGS

being potentially affected by aromatase inhibitor-induced arthralgia, or BIA being contraindicated in certain clinical scenarios - this protocol offers a structured approach to their use, supporting consistency and reliability. Importantly, the study has the potential to compare and validate HGS and WC against BIA, and to explore how these accessible tools correlate with clinical outcomes. In doing so, this work may provide an evidence base for inexpensive, scalable methods that can enhance dietetic practice and improve patient care.

Weight management in this patient cohort may be considered novel or even taboo among healthcare providers. Traditionally, weight maintenance or gain has been a key dietary goal during systemic anti-cancer treatment. Outside of the acute oncology setting, access to specialist oncology dietitians is often limited. Excess adipose tissue increases the risk of cancer recurrence, particularly in breast and gynaecologic cancer survivors, and raises the likelihood of chronic diseases such as type 2 diabetes and cardiovascular disease, the leading cause of death among postmenopausal women (73). A recent study of 1,000 women aged 50 years - 69 years found that 90% desired weight loss, and over 70% engaged in dieting behaviours (74). In Ireland, 37% of cancer survivors reported trying or following an alternative diet, while 30% avoided specific foods (28). These findings highlight the need for effective, sustainable weight management interventions that improve body composition and dietary quality. Such interventions could offer a three-fold benefit: reducing cancer recurrence risk, lowering chronic disease risk, and preventing harmful dieting behaviours.

The availability of oncology dietitians remains a challenge. In U.S. cancer centres, the patient-to-dietitian ratio is 1:2,380, with only 8.7% offering tele-dietetics or e-coaching (75). In Ireland, the ratio is even higher at 1:4,500 (76). Ireland has eight

designated cancer centres, with four in the capital, Dublin, and 14 additional centres with oncology or haematology consultants (8). The Irish Society of Clinical Nutrition and Metabolism reported that in 2019, only five full-time equivalent oncology dietitians worked outside the capital, and no dedicated dietetic survivorship services existed in any centre (8). Innovative and feasible pathways for dietetic intervention and support are being explored globally (77–80)**.** However, to our knowledge this is the first dedicated dietetic survivorship clinic based in an Irish regional cancer centre using ePROs to reach survivors in both rural and urban areas.

The sphere of telemedicine and telehealth has grown rapidly in the wake of COVID19 pandemic. If used effectively as a supplement to standard routine care, the use of electronic patient reported outcomes can allow healthcare professionals to closely monitor cancer survivors and related symptoms and intervene in a timely fashion. In 2023, a systematic review analysing over 15 randomised control trials (n = 2,363 cancer survivors) reported that mobile health dietary interventions may be an effective strategy for cancer survivors (81). The review reported significantly improved quality of life ($p = 0.04$), reduced weight ($p = 0.01$) and waist circumference ($p < 0.01$) (81). However, the trials included did not report lean body mass or fat tissue mass as an outcome (81). The trials conducted the interventions over a variety of timepoints; from 4 weeks to 24 months (81). Interestingly, only 3 RCTs reported interventions that were provided by a dietitian, other interventions were provided by cancer survivors, fully automated systems, medical students and unspecified healthcare professionals (81). The review concluded that larger scale RCTs with rigorous study design are needed to examine the effect of dietary interventions delivered via mobile health interventions.

The LYSA study design aligns with the EU Beating Cancer Plan which focuses on innovation, by tapping into the potential that digitalisation and new technologies offer.

Traditional survivorship care often relies on body weight or BMI as crude proxies for nutritional status which can mask important changes in lean tissue and fat distribution, especially in female cancer survivors exposed to endocrine therapy and iatrogenic menopause. This protocol addresses these limitations by incorporating BIA to assess body composition, offering a more sensitive and nuanced measure of nutritional status than weight alone; including muscle strength measurements to capture functional outcomes, which are critical indicators of sarcopenia and quality of life (56). The ability to track longitudinal changes in these parameters over 12 months, rather than relying on cross-sectional or self-reported data, is a significant strength to this protocol. Moreover, integrating body composition assessment within a comprehensive nutritional framework, including dietary intake, cancer-specific dietary quality, nutritional risk, and electronic patient reported outcomes, addresses a critical gap, as at the time of writing, no dietetic protocol encompassed this scope, or if one exists, it remains inaccessible due to lack of publication.

2.6 CONCLUSION

The LYSA randomised controlled trial represents a significant step toward addressing the gaps in survivorship care for early-stage breast and gynaecologic cancer survivors in Ireland. By integrating dietetic and nursing support with ePROs this study aims to provide a scalable, accessible model for a dietetic survivorship service. Given the impact of body composition and dietary quality on cancer recurrence and chronic disease, this protocol emphasises the importance of a comprehensive dietetic

assessment and intervention in this cohort. With limited access to oncology dietitians, the LYSA trial explores feasible dietary interventions and digital health strategies to enhance survivorship care. By aligning with the EU Beating Cancer Plan, this trial leverages innovation to improve patient outcomes and inform future models of care.

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CHAPTER 3: A COMPLEX SURVIVORSHIP INTERVENTION UTILISING ELECTRONIC PATIENT-REPORTED OUTCOMES IN BREAST AND GYNECOLOGIC CANCER: THE LINKING YOU TO SUPPORT AND ADVICE [*LYSA]* TRIAL

This work is has been published in the The Breast.

Johnston KE, O'Connell K, Raigal-Aran L, et al. A complex survivorship intervention utilizing electronic patient-reported outcomes in breast and gynecologic Cancer: the linking you to support and advice [LYSA] trial. Breast. 2026;86:104740. doi:10.1016/j.breast.2026.104740

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3.1 ABSTRACT

Background: Those living beyond a cancer diagnosis experience unmet supportive care needs due to fragmented post-treatment pathways and limited integration of digital health tools. The Linking You to Support and Advice (LYSA) trial assessed the feasibility of a complex-intervention which incorporated a dietitian- and nurse-led multidisciplinary clinic and a digital platform for capturing and responding to electronic Patient-Reported Outcome (ePRO) data for women with early-stage breast and gynaecologic cancer less than 12 months post-primary curative therapy.

Methods: The LYSA trial was an unblinded, randomised, controlled, feasibility trial co-designed with public and patient involvement, conducted across two cancer centres in Ireland. Participants were randomised to the experimental arm, receiving bi-monthly ePRO assessments and trigger-initiated responses to ePROs for 12 months; or the active comparator arm, receiving usual care. Primary feasibility outcomes included participant enrolment, ePRO survey completion, and healthcare professional engagement triggered by ePRO assessments. Secondary outcomes focused on symptom scores, health-related quality of life (HRQOL), and patient satisfaction. A process evaluation explored factors affecting implementation.

Results: The trial met its three predefined feasibility outcomes: 200 participants were enrolled (84% breast, 16% gynaecologic), >85% of baseline and endpoint surveys were completed, and >70% of participants in the experimental arm engaged in nurse and dietetic consultations following ePRO symptom triggers. The experimental arm demonstrated significant improvements in fatigue ($p = 0.018$), anxiety ($p = 0.012$), depression ($p < 0.001$) and HRQOL ($p = 0.031$) scores. The process evaluation indicated high levels of satisfaction with the intervention, with positive feedback on the multidisciplinary approach and responsive symptom management.

Conclusions: LYSA demonstrates the feasibility and acceptability of an ePRO-led survivorship approach, with potential HRQOL and symptom benefits, warranting a powered efficacy trial.

3.2 INTRODUCTION

Breast, cervical and endometrial cancers are within the top six female cancer cases diagnosed globally (1). In Ireland, female cancers (breast, cervical and endometrial) have relatively high overall 5-year net survival rates, currently at 88%, 65% and 78%, respectively (2). The estimated number of new cases of female cancers from 2022 to 2045 is projected to increase from 9.66 million to 15.2 million globally (3). Hormone-receptor positive breast cancers account for 70% of all female breast cancers diagnosed (4). Given the high prevalence of cancer diagnoses and unmet supportive care needs (5), there is a pressing need for coordinated care to ensure optimal patient outcomes and quality of life beyond the completion of primary treatment.

Despite recommendations from international oncology guidelines (6–11), standardised and individualised approaches to post-treatment supportive care are lacking; with a recent umbrella review (n = 123,411 participants) demonstrating that individuals affected by cancer continue to report that healthcare systems are not meeting their supportive care needs (12). Effective supportive care pathways should aim to improve outcomes in a sustainable, cost-effective and equitable manner while minimising the burdens on patients, caregivers and clinicians (13). Supportive care spans health promotion, chronic condition management, surveillance for recurrent and new malignancies, and the mitigation of physical and psychological effects of cancer and its treatment (14). Foundational frameworks by Nekhlyudov et al. (2019) (14) and Alfano et al. (2016) (15) have outlined principles for the delivery of high-quality survivorship care – emphasising coordination between providers, remote monitoring, triage algorithms and stakeholder engagement; as well as advocating for the

integration of evidence-based models across clinical, research, and policy domains (14).

Central to these models is the integration of digital health tools, including telehealth, electronic care plans, and electronic patient reported outcomes (ePROs), to enhance accessibility, personalisation and continuity of care (15,16). These insights have been reinforced in recent literature. Nekhlyudov et al. (2024) highlighted ongoing fragmentation in survivorship care and further underscored the role of digital innovation in enabling real-time symptom tracking, improving communication, and supported shared decision-making (17–20). Basch et al. (2005) introduced the feasibility of patient-reported symptom monitoring in cancer care, demonstrating improvements in communication, safety and clinical efficiency (21). Subsequently, Basch and colleagues noted that successful implementation of ePROs depend on process optimisation approaches that address key factors like software, leadership, workflow, deployment of personnel with roles changes to support ePROs, and patient engagement (22). Recently, a 2024 systematic review (n = 85 studies) emphasised the importance of innovating and integrating ePRO systems into cancer care pathways, supporting remote monitoring and optimising patient outcomes (23). When combined with evidence-based symptom management protocols and multidisciplinary collaboration, ePROs offer a promising approach to optimise outcomes for cancer survivors (24).

3.3 AIMS AND OBJECTIVES

Taking cognisance of this background, this chapter reports results of a randomised controlled trial (Linking You to Support and Advice: LYSA, NCT05035173) that assessed the feasibility of introducing a complex-intervention in two regional cancer

centres in Ireland. LYSA incorporated a dietitian- and nurse-led multidisciplinary clinic with ePRO technology to regularly collect and action symptom data for women with early-stage hormone receptor-positive breast, endometrial or cervical cancer. Data on usability, satisfaction and overall experience of the LYSA intervention and trial was collected as part of a mixed methods process evaluation.

3.4 METHODS AND MATERIALS

3.4.1 Patient and Public Involvement

A patient and public involvement (PPI) panel (n = 6), and clinical and academic stakeholders (n = 59) actively contributed to study design, implementation, and dissemination (25). Any patient-facing instrument was reviewed by the PPI panel, including surveys and symptom pathways. The research team and the PPI panel engaged in quarterly virtual meetings and received monthly email updates and were involved in the development of the accompanying lay summary [Supplementary Figure 3.1].

3.4.2 Study Design and Setting

The study protocol has been published previously (26). In brief, LYSA was an unblinded, randomised, controlled feasibility trial with parallel experimental and active comparator arms. Recruitment across two Irish cancer centres took place from 24th March 2021 to 23rd August 2022. Standardised reporting was supported through the use of the 2010 extension to the CONSORT (consolidated standards of reporting trials) for randomised pilot and feasibility trials (27) and the Practical Implementation Sustainability Model-Reach, Effectiveness, Adoption, Implementation, and Maintenance (PRISM-RE-AIM) framework (28).

The study was conducted in accordance with the Declaration of Helsinki and ICH E6 Good Clinical Practices and received full ethical approval from the relevant clinical research ethics committees [CREC Cork Teaching Hospitals ECM 3 08/12/2020; CREC Galway University Hospitals 121/21], with subsequent amendments approved as necessary.

3.4.3 Eligibility Criteria

Eligible participants included women with early-stage hormone-receptor positive breast, cervical or endometrial cancer within 12 months of completing primary curative therapy and with access to the internet. Participants were screened in medical oncology clinics. Consecutive eligible patients were approached. Eligibility was confirmed, and written consent was obtained by the research nurse, in person or remotely.

3.4.4 Intervention

The LYSA trial investigated the effect of a supportive care intervention, provided in response to changes in ePROs on HRQOL and symptoms experienced. Data were collected via the Castor Electronic Data Capture [EDC] platform (29).

Participants in the experimental and active comparator arms engaged in two in-person visits to the survivorship clinic (at baseline and end of study) and received a survivorship treatment summary and care plan at baseline (Figure 3.1). Both arms completed the ePRO Symptom, QoL and Nutritional Assessment Survey packages at baseline [T0] and end of study [T12] and had access to usual care. Usual care within the two centres followed national clinical guidelines for breast cancer care at the discretion of the primary team which usually includes six-monthly clinical follow up with an oncology provider, including medical, surgical, and radiation oncology

disciplines, annual breast imaging, and access to clinical nurse specialist support. Participants in both arms also had regular access to their primary care physician throughout the study period. Participants in the active comparator arm received enhanced usual care due to their engagement with the survivorship clinic at baseline and endpoint.

Participants in the experimental arm completed ePROs, including symptom assessment, every 2 months between baseline and end of study (Figure 3.1). ePRO survey responses activated an online trigger system that initiated prompt clinical follow-up by the nurse and/or dietitian, including virtual assessments by nurses and/or dietitians and shared symptom management using evidence-based care pathways. The intervention was broadly informed by Symptom Management Theory which views symptom care as a dynamic relationship between symptom experience, symptom management strategies, and associated outcomes (30,31). Detail of the full LYSA intervention is presented in the study protocol (26).

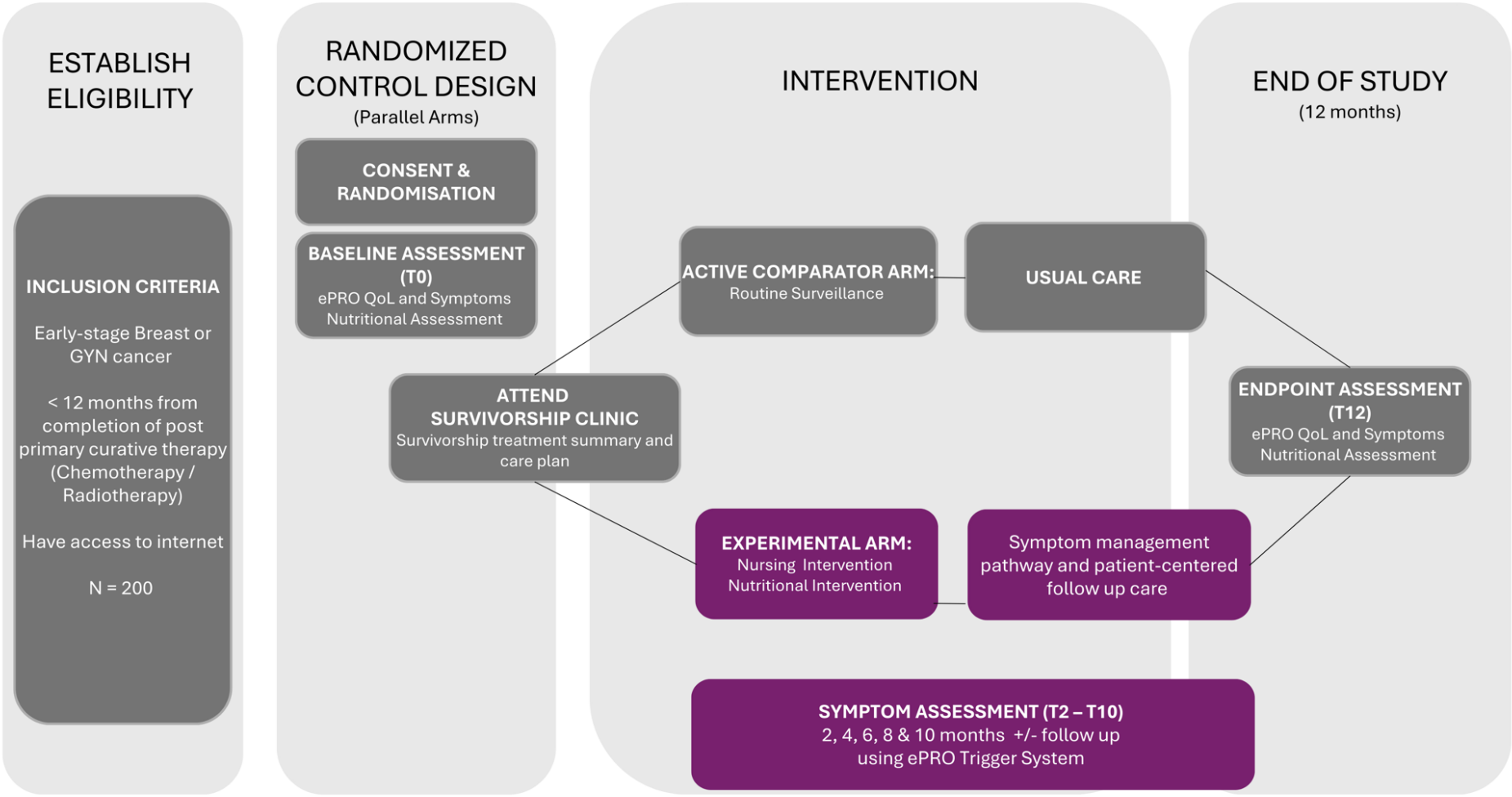


Figure 3.1: Trial Schema

Abbreviations: ePRO, electronic Patient Reported Outcomes; GYN, gynaecologic; QoL, quality of life.

3.4.5 Study Outcomes

The trial had three predefined primary feasibility outcomes:

(1) 200 participants enrolled;

(2) >50% of baseline and end of study ePRO surveys completed;

(3) following ePRO symptom triggers, >50% of participants engaged in nurse and dietetic consultations.

Secondary outcomes (exploratory efficacy outcomes) addressed in this manuscript relate to changes in electronic patient-reported symptom scores and HRQOL scores. As the study was not powered to detect differences, these outcomes are exploratory and hypothesis-generating and should be interpreted as same. Process evaluation outcomes were patient reported usability and satisfaction scores. Qualitative experiential data were also collected.

3.4.6 Additional Measures

The Symptom Survey ePRO package used items from the Patient Reported Outcome Measurement Information System (PROMIS) (33) and Common Terminology Criteria for Adverse Events (PRO-CTCAE) (34) to assess symptoms. In addition, fear of cancer recurrence, self-reported adjuvant endocrine therapy medication adherence, nutritional status and direct healthcare resource use were measured using researcher designed instruments and will be reported in future manuscripts. HRQOL was assessed using The European Organisation for Research and Treatment of Cancer Quality of Life (EORTC QOL) patient-reported core and disease specific measures (EORTC QLQ C30-Core and EORTC QLQ CX24, EN24, BR23) (35–38). Access to the electronic platform to complete the self-reported ePRO questionnaires was through a survey link sent to participants as required.

3.4.7 Sample size

The target sample size of 200 participants was a pragmatic figure, based on the desire to recruit the largest possible sample, given the expected number of eligible patients attending cancer centres during the time frame of the study (26). It was anticipated that this target sample size would provide a solid basis for identifying barriers to clinical implementation (39) and provide enough information on outcome distributions that would feed into the design of a subsequent, definitive efficacy trial (40,41).

3.4.8 Randomisation, Allocation Concealment and Blinding

Randomisation, conducted by the study's principal statistician, was stratified by cancer diagnosis in a 1:1 ratio for breast, cervical, and endometrial cancer using a computer-generated randomisation list using randomly sized blocks of size 4, 6, or 8 and operationalised via the study electronic data capture platform (Castor EDC). The allocations were concealed until patients were formally enrolled and consented into the trial. From that point forward, the study nurse and dietitian were not blinded to allocation, due to the nature of the intervention, and limited resources available for outcome assessor blinding. The study's principal statistician was blinded until the initial analysis of the study data were completed.

3.4.9 Data Management

Castor EDC allowed for data validation and metadata development throughout the study in accordance with the FAIR Guiding Principles for scientific data management and stewardship (42). Study metadata including data dictionary, data codebook and analysis scripts are available through the Open Science Framework repository (https://osf.io/y4wth/). Data sharing ethical approvals provide for future secondary

data use in cancer survivorship research. Requests for pseudonymised data access will be considered by the authors and in line with the General Data Protection Regulation (GDPR) and the Irish Health Research Regulations 2018 (43).

3.4.10 Statistical Methods

The feasibility endpoints of 1) percentage of baseline and endpoint surveys completed, and 2) percentage of participants engaged in nurse and dietetic consultations following ePRO symptom triggers were reported alongside 95% Wilson confidence intervals (CIs) (44) and compared to pre-registered progression criteria. Exploratory analyses were conducted for secondary outcomes. Between-arm differences in the end-of-study EORTC QLQ-C30 were estimated using complete-case samples using ordinal regression models with a logit link (i.e. a proportional odds model) (45). Ordinal models were chosen based on their ability to handle a variety of outcome distributions and because patient reported scores are not interval measures. Models were adjusted for baseline scores, and estimated effects were reported as odds-ratios (ORs) where values > 1 reflect better scores in the experimental arm relative to the active comparator arm. All effect estimates were reported alongside 95% CIs. Due to the exploratory nature of these analyses, there was no effort to adjust for multiplicity. PROMIS symptom scores were similarly analysed but coded in a manner such that ORs < 1 reflected a benefit in the experimental arm. All analyses were conducted using the R statistical programming language (version 4.4.1) (46) and the RStudio IDE (version 2024.12.0). Ordinal regression models were fit using the ordinal package (47). Other key packages included gtsummary (48) likert (49) and ggplot2 (50).

3.4.11 Process Evaluation

Embedded process evaluations are increasingly integrated into trials of health service interventions, offering crucial insights into the underlying processes; to clarify how interventions work, helping to interpret and contextualise study findings (51,52). An in-depth qualitative descriptive approach, using semi-structured one-to-one interviews, was employed to explore experiences of the LYSA intervention and trial processes. Patients, healthcare professionals, stakeholders, and members of the PPI panel were invited to participate in post-trial interviews and were provided with participant information and consent materials. As outlined in the participant information leaflet, patients who expressed interest could opt in to a one-to-one interview. From those who consented to be contacted, a purposive sample of twenty patients was selected to ensure variation across study arms and participant characteristics and experiences of the intervention. Study team members (n = 7), stakeholders (n = 4), and PPI panel members (n = 7) were recruited using purposive and/or convenience sampling to capture a range of perspectives on implementation and trial processes.

Interviews were conducted by an independent researcher via MS Teams, lasted 15-60 minutes, were audio-recorded with consent, transcribed verbatim, anonymised, and securely stored. A flexible semi-structured topic guide was used, allowing participants to discuss issues of importance while ensuring coverage of key evaluation domains. Across all participant groups, interview guides explored: (i) experiences of the LYSA intervention or trial processes, (ii) acceptability and usability of intervention components, (iii) experiences of the electronic patient-reported outcome (ePRO) system, (iv) perceived facilitators and barriers to implementation, (v) impact on care

delivery, and (vi) recommendations for future implementation and sustainability. Patient-specific guides additionally explored timing, duration, and burden of follow-up care and comparisons with routine care. Healthcare professional, research team, and stakeholder guides focused on implementation fidelity, resource use, workflow integration, and service delivery barriers and facilitators. An online survey distributed via Castor EDC captured additional quantitative data on usability and satisfaction among trial participants. The survey included items assessing usability of the ePRO system (e.g. ease of use, interface design, clarity of information, and time burden) as well as satisfaction with key components of the LYSA intervention and trial processes. Responses were recorded using a five-point Likert scale and subsequently collapsed into three categories (agree, neither agree nor disagree, and disagree) for analysis. In the experimental arm, additional items assessed satisfaction with specific intervention components, including survivorship clinic consultations, personalised care planning, symptom monitoring, and access to follow-up care. These were used to support triangulation with qualitative findings.

Transcripts were analysed inductively using Graneheim and Lundman's qualitative content analysis (53), which involved systematically reading raw data to create codes (labels for meaning units), grouping similar codes into subcategories, and then further organizing these into broader categories to reveal patterns or themes emerging from the data without preconceived theories. Separately, the PRISM (RE-AIM) framework was used to deductively organise implementation factors (28). Rigour was supported through peer validation, rich contextual description, use of exemplar quotes, and adherence to principles of credibility, transferability, dependability, and confirmability (54).

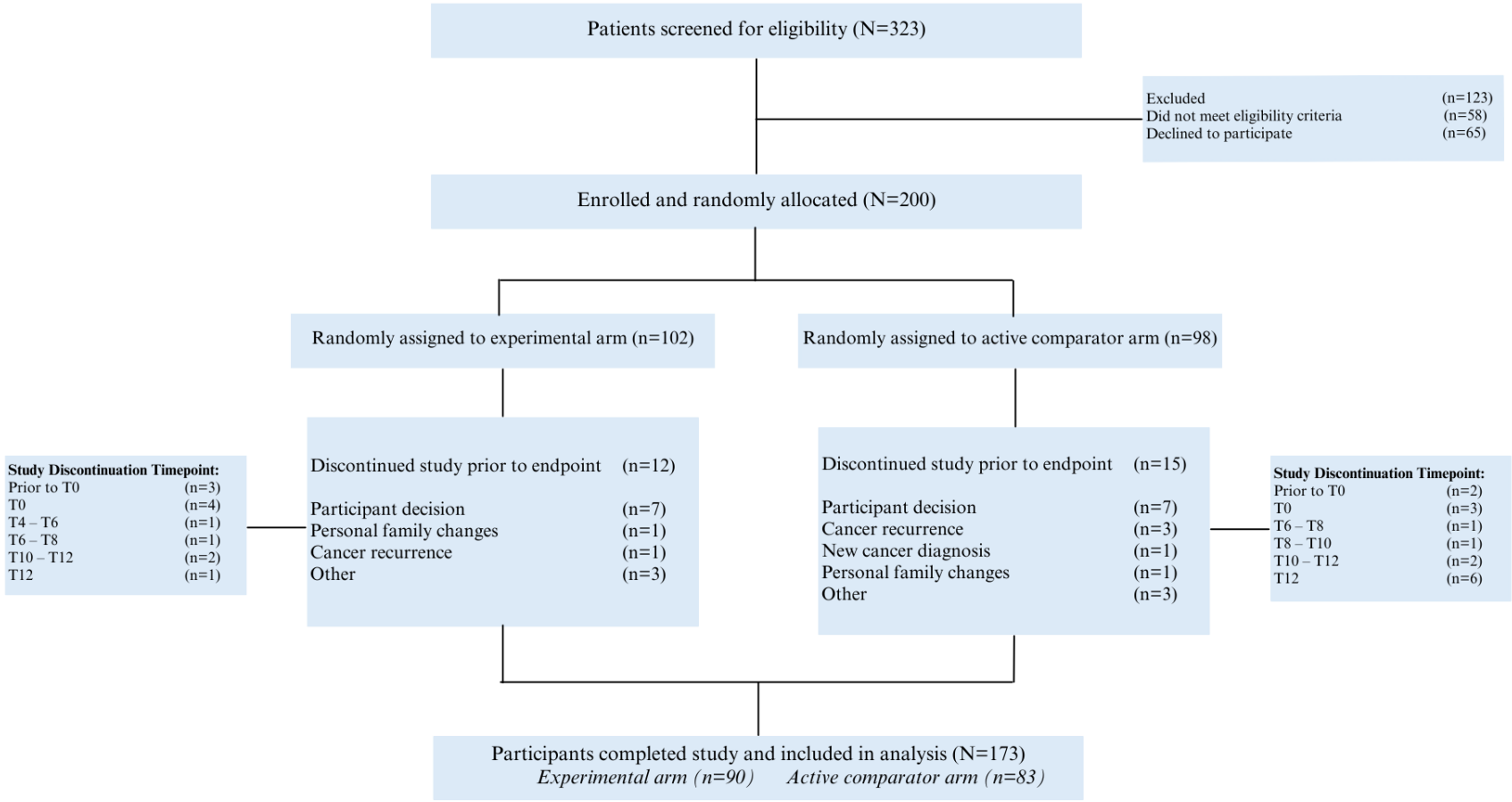


Figure 3.2: CONSORT Diagram

3.5 RESULTS

3.5.1 Participant Characteristics

Of 323 potential participants screened, 200 women were randomised to the trial across two sites, meeting the first predefined feasibility outcome (Figure 3.2). Over the 18-month recruitment period, 323 patients were screened, representing an enrolment rate of 61.9% and an average recruitment rate of 11.1 participants per month. Of the 123 patients not enrolled, 58 were ineligible and 65 declined participation. The most commonly documented reasons for declining participation related to competing personal commitments (n = 23), perceived hospital burden (n = 12), travel requirements (n = 3), and return-to-work commitments (n = 2), suggesting that practical barriers rather than lack of interest may have influenced participation decisions.

Baseline clinicopathologic and treatment characteristics by study arm are provided in Table 3.1 and sociodemographic characteristics in Supplementary Table 3.1. The timeframe of the trial coincided with the COVID19 global pandemic, and a national public health service (Health Service Executive) cyberattack. COVID19 precipitated the use of virtual consent processes and e-consultations. A total of 86.5% (n = 173) of participants completed the trial [Figure 3.2]. Reasons for study discontinuation included participant decision (n = 18), cancer recurrence (n = 4), new cancer diagnosis (n = 1) and other (n = 4) [Supplementary Table 3.2].

TABLE 3.1: Baseline Clinicopathologic and Treatment Characteristics of all Randomised Participants

Characteristic	N	Overall	Active Comparator	Experimental
		N = 200	N = 98	N = 102
Age in years (median, range)	192	54 [23 to 78]	55 [31 to 78]	54 [23 to 75]
Cancer diagnosis	195			
Breast		164 (84%)	83/96 (86%)	81/99 (82%)
Cervical		13 (6.7%)	5/96 (5.2%)	8/99 (8.1%)
Endometrial		18 (9.2%)	8/96 (8.3%)	10/99 (10%)
Menopausal status	195			
Pre		61 (31%)	28/96 (29%)	33/99 (33%)
Peri		20 (10%)	7/96 (7.3%)	13/99 (13%)
Post		110 (56%)	57/96 (59%)	53/99 (54%)
Unknown		4 (2.1%)	4/96 (4.2%)	0/99 (0%)
ECOG performance status	194			
0		64 (33%)	31/96 (32%)	33/98 (34%)
1		125 (64%)	62/96 (65%)	63/98 (64%)
2		5 (2.6%)	3/96 (3.1%)	2/98 (2.0%)
Prior Surgery	195	186 (95%)	91/96 (95%)	95/99 (96%)
Prior Radiotherapy	195	192 (98%)	94/96 (98%)	98/99 (99%)
Prior Chemotherapy	*194*	119 (61%)	57/96 (59%)	62/98 (63%)
Prescribed Endocrine Therapy	195	163 (84%)	83/96 (86%)	80/99 (81%)
Aromatase Inhibitor *		90/163 (55%)	45/83 (52%)	45/80 (60%)
Tamoxifen		59/163 (36%)	32/83 (39%)	27/80 (34%)
*Aromatase Inhibitor */ Tamoxifen with Ovarian Function Suppression*		14/163 (9%)	6/83 (7%)	8/80 (10%)

* Aromatase Inhibitors include: Anastrozole, Exemestane and Letrozole

Abbreviations: ECOG, Eastern Cooperative Oncology Group

3.5.2 Primary Feasibility Results

In addition to enrolling all 200 participants as planned, 96.5% of participants completed the baseline ePRO Symptom Survey package (193/200, [*95% CIs: 93 to 98%*]), while 89% completed the end of study survey (178/200, [*95% CIs: 84 to 93%*]), thus exceeding the benchmark of >50% of baseline and endpoint ePRO surveys completed [Supplementary Table 3.3]. The final predefined requirement to confirm feasibility of the LYSA intervention stipulated that >50% of participants engaged in nurse and dietetic consultations following ePRO symptom triggers. Following an ePRO symptom trigger in the experimental arm [Supplementary Figure 3.2], 84% (*95% CIs: 76 to 90%*) and 72% (*62 to 79%*) of participants engaged with nurse and dietetic consultations, respectively. Nurse and dietitian consultations were initiated through three possible mechanisms: symptom(s) trigger (n = 565) [Supplementary Table 3.4]; patient-initiated request for call back (n = 61); or nurse or dietitian's clinical judgement based on overall symptom profile (n = 0).

There were 322 nurse virtual visits initiated by symptom triggers (involving 86 participants), and a further 47 virtual nurse visits due to patient-initiated request for call back (27 participants). In relation to dietetic consultations, there were 243 virtual visits initiated by symptom triggers (73 participants), and a further 14 virtual visits due to patient-initiated request for call back (11 participants). The median length of in-person nurse visits was 60 minutes (interquartile range [IQR] 45-60), while it was 90 minutes for in-person dietitian visits (IQR 70-120). For symptom-trigger initiated consultations (T2-T10), the median length of a nurse consultation was 35 minutes (IQR 20-60), and for dietitian consultations, 40 minutes (IQR 30-75). The trigger-

initiated consultations (T2-T10) equated to 39.1 hours of nursing services and 57.8 hours of dietetic services.

There were 28 medical reviews required by 25 participants, that were prompted by consultation with the research nurse; mean time to medical consultation was 2.4 days (standard deviation (SD) ±8.8; range [days] 0-46). Reasons for medical review included the need for physical examination based on reported symptoms (n = 5); new (n = 2) or worsening (n = 8) symptoms requiring physician input; the need for endocrine therapy (n = 2) or supportive medication prescriptions (n = 8).

TABLE 3.2: Standardised EORTC-C30 Scores at Study End (T12) with Estimated Treatment Effects

Characteristic	**Study Arm (N=162)**		**Odds ratio (95% CI)**[+]	**p-value**
	Active Comparator N = 76[^]	**Experimental** N = 86[^]		
EORTC C30 global health status score	53 (18); 50 [42, 67]	55 (18); 50 [50, 67]	1.26 (0.72 to 2.2)	0.42
EORTC C30 physical functioning score	81 (20); 87 [73, 93]	86 (14); 87 [80, 100]	1.7 (0.97 to 3.03)	0.067
EORTC C30 role functioning score	68 (32); 67 [50, 100]	79 (23); 83 [67, 100]	1.96 (1.09 to 3.58)	**0.026***
EORTC C30 emotional functioning score	67 (23); 71 [50, 83]	74 (17); 75 [67, 92]	1.61 (0.92 to 2.82)	0.098
EORTC C30 cognitive functioning score	67 (28); 67 [50, 83]	70 (22); 67 [50, 83]	1.27 (0.72 to 2.25)	0.42
EORTC C30 social functioning score	73 (25); 67 [67, 100]	79 (20); 83 [67, 100]	1.66 (0.93 to 2.99)	0.088

EORTC C30 fatigue score	64 (22); 67 [56, 78]	69 (20); 67 [56, 89]	1.57 (0.9 to 2.75)	0.11
EORTC C30 nausea and vomiting score	90 (18); 100 [83, 100]	94 (10); 100 [83, 100]	1.58 (0.78 to 3.22)	0.2
EORTC C30 pain score	68 (28); 67 [50, 100]	73 (25); 83 [50, 100]	1.46 (0.83 to 2.56)	0.19
EORTC C30 dyspnoea score	83 (23); 100 [67, 100]	86 (18); 100 [67, 100]	1.1 (0.55 to 2.17)	0.79
EORTC C30 insomnia score	59 (32); 67 [33, 100]	62 (26); 67 [33, 67]	1.52 (0.84 to 2.78)	0.17
EORTC C30 appetite loss score	89 (21); 100 [100, 100]	89 (20); 100 [67, 100]	0.77 (0.35 to 1.66)	0.5
EORTC C30 constipation score	77 (27); 100 [67, 100]	82 (26); 100 [67, 100]	1.72 (0.9 to 3.33)	0.1
EORTC C30 diarrhoea score	89 (22); 100 [67, 100]	92 (16); 100 [100, 100]	1.47 (0.67 to 3.26)	0.34
EORTC C30 financial problems score	80 (28); 100 [67, 100]	84 (24); 100 [67, 100]	1.93 (0.92 to 4.12)	0.084
EORTC C30 summary score	75 (16); 77 [67, 88]	80 (13); 82 [71, 89]	1.83 (1.06 to 3.18)	**0.031***

^ Mean (SD); Median [Q1, Q3]

+ Treatment effect estimated using complete-case, baseline-adjusted ordinal regression

*** p < 0.05**

Abbreviations: CI, Confidence Intervals; EORTC, European Organisation for Research and Treatment of Cancer

3.5.3 Secondary Outcomes (Exploratory Efficacy Outcomes)

Between-arm differences in end-of-study EORTC QLQ-C30 scores are shown in Table 3.2 and disease specific scores in Supplementary Table 3.5. Findings suggest that participants in the experimental arm experienced better EORTC QLQ-C30

summary scores (*p = 0.031*) and role functioning (*p = 0.026*) when compared to patients in the active comparator arm (baseline-adjusted OR 1.83, 95% CI 1.06 to 3.18; 1.96 (1.09 to 3.58). Fourteen of the fifteen remaining sub-scores (the outlier being appetite loss) had treatment effect point-estimates that suggested a benefit for the experimental arm relative to active comparator, though 95% CIs were typically wide. Between-arm differences in end-of-study PROMIS symptom scores are shown in Table 3.3. Treatment effect estimates suggested lower, better symptom scores for fatigue (OR 0.53, [*95% CI 0.31 to 0.89*]), anxiety (0.5, [*0.29 to 0.86*]) and depression (0.36, [*0.2 to 0.64*]), but not for vaginal discomfort, in the experimental arm relative to the active comparator arm.

TABLE 3.3: Standardised PROMIS Scores at Study End (T12) with Estimated Treatment Effects

PROMIS standardised score	N	Study Arm		Odds ratio (95% CI) [+]	p-value
		Active Comparator N = 82[^]	Experimental N = 90^		
Fatigue	172	53 (10); 52 [46, 61]	50 (9); 50 [46, 57]	0.53 (0.31 to 0.89)	**0.018 ***
Vaginal discomfort	74	48 (7); 48 [45, 51]	46 (7); 48 [41, 51]	1.17 (0.43 to 3.24)	0.754
Missing values [~]		46	52		
Anxiety	172	57 (9); 58 [51, 63]	53 (8); 56 [48, 58]	0.5 (0.29 to 0.86)	**0.012 ***
Depression	172	53 (9); 54 [40, 59]	48 (8); 45 [40, 56]	0.36 (0.2 to 0.64)	**< 0.001 ***

[^] Mean (SD); Median [Q1, Q3]

+ Treatment effect estimated using complete-case, baseline-adjusted ordinal regression; OR < 1 suggests benefit in the experimental arm relative to the active comparator arm

*** p ≤ 0.05**

[~] Missing values (n = 98) denote participants who had not had sexual intercourse in the last 30 days

Abbreviations: CI, confidence intervals; PROMIS, Patient-Reported Outcomes Measurement Information System

3.5.4 Process Evaluation

Qualitative interviews were conducted with twenty study participants, seven study team members, four stakeholders and seven PPI panel members. Study participants were women with breast cancer from the experimental arm (n = 14) and active comparator arm (n = 6). Notably, whilst open to all participants, no patients with gynaecologic cancers participated in the process evaluation interviews. Two categories and twelve sub-categories are presented in Table 3.4, which highlight the positive and negative aspects of the LYSA intervention and trial and provide recommendations for future implementation.

Important findings from the process evaluation include that the LYSA intervention addressed the sudden reduction in contact and support at the end of treatment, at a time when the patient is vulnerable, by providing a clear pathway for managing symptoms and issues. Having a dedicated clinical and ePRO system changes the lens from hospital and treatment to living well beyond cancer. Key positives included patients feeling that they were connected into the hospital from their home; feeling supported giving participants' confidence; feelings of affirmation by having symptoms and issues listened to; and providing continuity of care. One health care professional noted "*They [the patient] won't necessarily bring that [decreased libido] up and certainly won't discuss it at a clinical visit …. But in this [survey] it's triggered for an awful lot of women, and it is because they're allowed to ask the question.*".

There was a high degree of consensus among experimental arm participants regarding the intervention's usability and acceptability [Supplementary Table 3.6]. However, 56% of participants indicated a preference for technology-based questionnaires over

traditional paper formats, highlighting both a growing comfort with digital health tools and a cohort of individuals who are more comfortable with paper-based surveys.

Positive and negative implementation factors linked to implementation of the LYSA trial were coded to the PRISM (RE-AIM) framework allowing the team to explore and understand the factors that influenced the implementation of the intervention in a real-world context [Supplementary Table 3.7]. Key influencing factors included: enabling national policy; service level support; partners and relationships; co-design; funding, resources and infrastructure; digital infrastructure; digital capabilities of patients; and having symptom specific pathways.

Table 3.4: LYSA Process Evaluation Categories, Sub-Categories and Codes

Main categories ^	Sub-categories	Codes
Positive and negative aspects of the LYSA intervention	Enhanced supportive care services different from usual care	Intervention addresses the sudden reduction in contact/support at the end of treatment, at a time when the patient is vulnerable
		Intervention provides pathway for managing symptoms and issues
		Clinic services in one place
	Positive aspects of the LYSA clinic	Mindset of survivorship rather than hospital and treatment, helping individuals to live better beyond cancer
		Supported connecting out (from hospital); accessible from own home and feeling connected in (to hospital)
		Felt supported, supportive and practical intervention
		Tailored to individual needs
		Ensures continuity of care
		Positive impact on health and wellbeing
		Timing of intervention right
		Well-run clinic
	Positive aspects of the LYSA serial electronic surveys	Helped to link in, someone available to review
		Breadth of survey- coverage of symptoms broad
		Self-check-in with surveys
		Progress recorded, giving confidence
		Easy to do and user friendly
		Quick, no pressure

Main categories ^	Sub-categories	Codes
	Positive aspects of LYSA trigger system	The trigger system works well; the dietitian and nurse can follow a patient together
		Patient can organise joint visits with dietician and nurses
		Facilitates MDT referral pathway.
	Positive aspects of managing symptoms	Early management of symptoms and side effects of treatments outside of usual surveillance focused pathway e.g. tamoxifen or dealing with symptoms that worsened over time
		Provided a mechanism of sharing details on topics and issues that were perceived to be difficult to talk about e.g. sharing difficulties with sexual health
		Provided advice and support for ongoing symptoms and issues e.g. lymphoedema
		Provided a solution when some [patients] perceived that their GP [family physician] was not familiar with or understanding of symptoms
		Affirmation of having symptoms and issues listened to
	Other positive aspects	Promoted focus on health and well being
		Kept patients out of the emergency department and hospital
	Negative aspects of the LYSA survey	Some unclear survey questions- perception [by some] that there was a right answer
		Repetition and relevance of some survey items
		Dietetic baseline and end of study assessments take a lot of time to complete
	Negative aspects of LYSA trigger system	Time taken to review triggers and identify those triggers that must be seen by a health care professional
		Sensitivity and specificity of some triggers: some triggers impacted by multi-morbidities (e.g. irritable bowel disease); lack of triggers for person below healthy BMI or in the healthy BMI range but gaining weight
	Negative aspects of LYSA clinic	No specific LYSA team support at weekends or at night
		Symptom management pathways too generic
		Negative aspects of onward referrals e.g. increased waiting time for patients accessing certain services

Main categories ^	Sub-categories	Codes
Recommendations	Positive aspects of LYSA HCPs	Built relationships with nurse and dietician over time
		Nurse – "the go to" person; available, knowledgeable, kind person who can give extra advice/support, assist with system navigation to sort issues out
		Patients felt that they had someone to confide in; a champion
		Dietitians were educators, providing good, practical nutritional advice and resources e.g. cookbook to help patients make changes in their diet
		Lots of support and information
	Negative aspects of LYSA HCPs	More empathy for where the patient is at in their individual journey
	Clinic and Survey and services	Timing of clinic- start 2-3 months after treatments completed, and continue for longer, maintain contact for longer than one year with access based upon need
		Clinic- include more face-to-face options, perhaps consider a community-based setting
		Review survey to reduce repetition and length
		Consider paper and digital surveys for those with limited digital capabilities
		Refine survey triggering levels and healthcare professional response mechanisms
		Revise communication/triggering system from using emails to a summary statement/ record that can be easily checked within the patients' health record
		Provide feedback to GP [family physician]
		Automated feedback to patients on symptoms experienced in survey e.g. visuals or graph to show progress to the patient, provide online feedback
		Access to more of services/ interventions in the community closer to the patient; referral based upon local zip code/GPS or local cancer support services e.g. community physiotherapy services, exercise classes
		Fully integrated service with everything in one building- 'One stop shop' with all services available including genetics for in person visits

Main categories ^	Sub-categories	Codes
		Be more family centred - include family and children
		Extend LYSA to include opportunity for a clinic for women with advanced or metastatic cancer
		More supports re return to work and entitlements
		More help in navigating mental health e.g. fear of cancer recurrence
		Increase access to counselling/ psychologist/cognitive behavioural therapy
		Recommend peer support group to talk/ meet others to feel less isolated

^ Codes, subcategories, and categories emerging from indictive analysis of interview data.

3.6 DISCUSSION

This randomised controlled trial of the 12-month LYSA intervention met its three predefined feasibility outcomes, with 200 women enrolled, an 86.5% study completion rate and high engagement with healthcare professionals following ePRO triggers. Predefined secondary objectives also suggested potential efficacy of the LYSA intervention; however, these should be interpreted with caution due to the exploratory nature of the analyses. Favourable outcomes were observed in the experimental arm when compared to the comparator arm, particularly in relation to fatigue, anxiety, and depression symptom scores whilst acknowledging that the study was not powered to test efficacy of the intervention. Furthermore, the LYSA intervention was reported to be highly acceptable to participants, healthcare professionals, PPI partners and stakeholders alike, suggesting that next step investigations of the LYSA intervention can be successfully conducted.

Our findings align with existing research (15,18,23,55) reinforcing established trends and supporting frameworks (16,17,56) for integrating symptom monitoring and ePROs into clinical workflows as a supplement to routine survivorship care. Since the inception of this trial, a key umbrella review of systematic reviews (n = 222 unique studies) evaluating the effects of patient reported outcome measures (PROMs) feedback was published (57). Umbrella review authors highlighted PROM feedback consistently enhanced aspects of care processes such as communication and the recognition and management of symptoms (57). However, the evidence regarding its impact on patient health outcomes was less definitive. While 60% (n = 12) of systematic reviews reported promising interventions, results were mixed; particularly for quality of life (n = 7 reported as effective) and psychological symptoms such as anxiety and depression (n = 5 reported unchanged symptoms) (57). The LYSA

intervention suggests preliminary efficacy across multiple domains and quality of life, however a definitive, fully powered trial should be conducted to establish these effects. Through the process evaluation, the research team attribute much of this potential benefit to its multidisciplinary approach, centralised point of contact, and responsive design enabled by targeted ePRO triggers.

A strength of this feasibility trial design was in the inclusion of a process evaluation. The implementation of complex health interventions such as LYSA into dynamic, multi-level healthcare systems, particularly in hospitals, is inherently complex and multifactorial. The integration of a digital workflow adds another layer of complexity, requiring the collaboration of various stakeholders, including clinical professionals, administrative staff, researchers, and community partners. This complexity is evident when considering the positive and negative implementation factors associated with frameworks like PRISM (RE-AIM), which reflect various domains, such as Reach, Efficacy, Adoption, Implementation, and Maintenance. These factors, along with the significant resource use of nursing and dietetic services, will require dedicated survivorship programs and staff if implementing into healthcare pathways. A future economic analysis of the LYSA intervention will provide tangible data for cost and resource implications.

The LYSA trial represents a significant advancement in digital survivorship care in Ireland, leading to new real-world data in enhanced supportive care. Conducted across two large Irish cancer centres and including participants from both rural and urban areas, the study provides a robust model for scaling ePRO-driven interventions, and aligns with international digital health strategies such as the EU Beating Cancer Plan (56) and the US 21st Century Cures Act (58). The randomised design has allowed

preliminary comparison between arms which will guide a fully powered randomised controlled trial.

An additional strength of this trial was the formation of a summative one page, traffic light colour coded patient-reported symptom list to guide clinical consultations [Supplementary Figure 3.2]. This was a practical tool for multidisciplinary teams to monitor symptoms and provide timely intervention to the growing population of cancer survivors. The longitudinal nature of the LYSA intervention and the serial ePRO collection provided a unique picture of the symptom profile and needs. By enabling nurses and dietitians to collaborate effectively, this digital model recognised that symptoms do not occur in isolation but affect physical, psychological, nutritional, and functional status. Future research should aim to expand on the longitudinal nature of the LYSA intervention, acknowledging that not all symptoms arise in the first-year post-treatment but can occur into long-term survivorship.

The integration of ePROs with electronic health records remains a key challenge. In Ireland, emerging research, such as the LYSA trial, may strengthen the integration of PROMs into a developing national electronic health record. Current literature supports the role of symptom monitoring in enhancing patient engagement, enabling timely interventions, and reducing adverse events among cancer survivors (18,19,55,57,59–61). However, harvesting large data sets from ePROs within existing hospital systems remains a barrier. Approximately 70% of ePRO systems in survivorship care remain independent of hospital electronic health records, reducing their full potential for system-wide analytics (55). Looking ahead, the integration of artificial intelligence (AI) driven algorithms and predictive scoring tools, overseen by healthcare and medical professionals, could further optimise ePRO use, enabling

smarter, more personalised survivorship care. The establishment of a colour-coded trigger alert system in the LYSA trial is a welcome step towards generating assisted prompts for timely, targeted and patient-centred survivorship supportive care.

A few limitations to the LYSA study design must also be acknowledged. The trial focused on three female cancer subtypes (breast, cervical, endometrial) with similar symptom profiles and pathways; limiting generalisability to other cancer types. However, the study intervention could easily be investigated in other cancer populations, including metastatic cohorts, using learnings from this study. Secondly, participants required internet access to meet eligibility criteria based on the ePRO platform we utilised, potentially excluding digitally underserved populations. Thirdly, the trial was not powered to detect difference in efficacy outcomes. However, the findings lay the foundation for a fully powered definitive trial. Furthermore, the active comparator arm's exposure to survivorship clinics, survivorship care plans and repeated PROMs may have functioned as enhanced usual care, thereby attenuating observed differences between the two groups. Another limitation was the 14% drop out rate in the study. Our exploratory, complete-case analyses of efficacy outcomes assume that values are missing completely at random (MCAR) and thus could be biased in the presence of differential loss to follow up. That said, drop-out rates were similar in both arms (15% of control and 12% of active arm participants) and there were no statistically significant differences in key baseline characteristics in those who dropped out versus those who completed the study. Finally, although all patient-facing materials were co-designed with the LYSA PPI panel, the potential burden of lengthy symptom questionnaires may be a concern for broader implementation.

Whilst evidence is robust for survivorship care interventions similar to LYSA, sustained evidence of their implementation and translation into routine clinical practice is lacking. The LYSA trial has, however, informed and prioritised survivorship care in these regional cancer centres in Ireland. Future LYSA trial outputs will include an economic analysis, providing data for service development and strategic planning to assist in meeting growing demands for supportive care on the cancer journey. Future research should explore how AI-generated responses, predictive scores, and adaptive algorithms, overseen by clinical experts, can further optimise ePRO systems within cancer centres. By leveraging digitalisation, ePROs can inform more inclusive, targeted, efficient and data-driven survivorship care for future generations.

3.7 CONCLUSION

To conclude, the LYSA trial met its primary feasibility endpoint, demonstrating that a complex survivorship intervention incorporating ePROs is feasible and acceptable in routine follow-up care for patients with early-stage breast and gynaecologic cancer. High completion rates of ePRO surveys and substantial engagement in symptom-triggered healthcare consultations were observed. The experimental arm suggested better symptom management and QOL outcomes, highlighting potential benefits of the intervention. In line with the Medical Research Council's guidance on the development and testing of complex interventions (51), a future definitive randomised controlled trial should build on the outcomes of the LYSA feasibility trial.

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CHAPTER 4: EVALUATION OF TRIGGER-INITIATED VIRTUAL DIETETIC CONSULTATION VIA EPROS ON ENGAGEMENT, BODY COMPOSITION AND DIETARY QUALITY IN BREAST AND GYNAECOLOGIC CANCER SURVIVORS: *RESULTS FROM THE LYSA RANDOMISED CONTROLLED TRIAL*

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4.1 ABSTRACT

Background: Breast and gynaecologic cancer survivors often experience weight gain, adverse body composition changes, and unmet nutritional needs. Weight stigma further limits engagement with care, while dietetic services remain reactive and underutilised. Electronic patient-reported outcomes (ePROs) offer a novel, patient-centred approach to initiate timely dietetic support, but their use in survivorship care is largely unexplored.

Methods: The unblinded, randomised controlled LYSA Trial was conducted in two Irish cancer centres with early-stage breast and gynaecologic cancer survivors who had completed curative therapy within the past 12 months. Participants were randomised 1:1 to an experimental arm, receiving two-monthly ePRO surveys with trigger-initiated virtual dietetic consultations plus personalised counselling, or an active comparator arm receiving routine care. The ePRO system generated triggers based on body mass index (BMI), Malnutrition Screening Tool (MST) score and patient reported weight gain concern. Baseline and 12-month assessments included body composition, dietary quality (World Cancer Research Fund [WCRF] adherence score), and nutritional risk screening and patient-reported weight-gain concern. The primary outcomes were the implementation and engagement with the trigger-based dietetic system; secondary outcomes were changes in body composition and dietary quality (WCRF adherence score).

Results: Of 325 patients screened, 200 were enrolled (experimental n = 102; comparator n = 98), with 173 (86.5%) completing the 12-month trial. MST triggers were reported in <10% of participants and decreased slightly by endpoint, while BMI triggers were more common (experimental 60%; comparator 47%) and remained

stable. In the experimental arm, 76.6% of dietetic consultations were symptom-triggered, with 40.5% of participants initiating five consultations; 27.8% of consultations were not attended, primarily due to participants declining or being unreachable after multiple contacts. Body composition remained stable, with no significant differences in weight, BMI, waist circumference, lean or fat tissue indices, or handgrip strength. Patient-reported weight gain concern decreased in the experimental arm (58.8% to 46.7%) versus an increase in the comparator arm (62.7% to 68.7%; $p = 0.01$). Dietary quality scores showed small improvements in red and processed meat and sugar-sweetened beverage adherence recommendations in the experimental arm, with higher trigger counts associated with lower overall adherence scores (r = -0.364 to -0.532, $p < 0.001$).

Conclusion: A trigger-based, ePRO-initiated dietetic intervention was feasible, acceptable, and reduced patient-reported weight gain concern among early-stage breast and gynaecologic cancer survivors, despite minimal changes in body composition or dietary quality. Engagement with the symptom-responsive consultation model highlights the potential for personalised dietetic support to address weight- related concerns in survivorship care. These findings inform the development of standardised, resource-efficient, survivorship-specific dietetic services and warrant fully powered trials to optimise long-term dietary and psychosocial outcomes.

Clinical Trial Registry: ClinicaTrials.gov [NCT05035173]

4.2 INTRODUCTION

Globally, the burden of cancer is rising, with female cancer incidence projected to increase by over 55% by 2045 (1). In Ireland, breast, cervical, and endometrial cancers are expected to rise substantially, exceeding European averages, reflecting an urgent need to support growing survivorship populations (1). Advances in early detection and treatment mean that more individuals are living beyond a cancer diagnosis, yet these survivors often experience complex late and long-term effects of treatment, including physical, psychological, and nutritional challenges (2). When survivorship care addresses these multidimensional needs, patients are more likely to transition from a state of illness to sustained health (2).

Breast and gynaecologic cancer survivors report high prevalence of unmet supportive care needs, yet standardised multidisciplinary care remains limited (3,4). Guidelines from the National Comprehensive Cancer Network (NCCN) and the American Cancer Society highlight the importance of optimising body composition and managing treatment-related nutritional challenges (5,6). These issues are particularly relevant for hormone-receptor positive breast cancer survivors on endocrine therapy and for those experiencing iatrogenic menopause, both of which can profoundly affect body composition, metabolism, and dietary behaviours (7). Despite these risks, survivors often report receiving minimal support from healthcare providers for symptom- or treatment-related nutritional concerns (7).

Weight gain and changes in body composition are critical survivorship concerns. Adiposity is associated with increased recurrence risk and cardiovascular morbidity, even among individuals with a healthy body mass index (BMI) (8,9). In survivors receiving adjuvant endocrine therapy, weight gain is common: prevalence ranges from

18% to 52% in the first year and 7% to 55% by the fifth year post-diagnosis, with recent evidence linking ≥10% post-diagnosis weight gain to a 23% higher mortality risk (10,11). Effective management is complex and multifactorial, often complicated by pervasive weight stigma. Cancer survivors living with obesity report discrimination and bias across the care continuum, which undermines engagement with healthcare and adherence to lifestyle interventions (12,13). These findings highlight the need for interventions that address both physiological and psychosocial aspects of weight management in a patient-centred, non-stigmatising manner.

Dietitians play a central role in delivering personalised, multifaceted interventions to improve dietary quality, weight management, and health outcomes in cancer survivorship (14). Evidence from primary care dietetic interventions show benefits for weight, dietary quality, biomarkers and, in some cases, quality of life (14). However, existing services are largely reactive, limited in accessibility, and often insufficiently tailored to the complex needs of breast and gynaecologic cancer survivors (15,16) Despite high demand, breast cancer survivors remain among the least likely to receive dietetic support (15) and dietitians report challenges including care coordination, lack of dedicated resources, and poor integration into multidisciplinary teams (16).

Digital tools, particularly electronic patient-reported outcomes (ePROs), offer a promising solution to these challenges. ePROs facilitate real-time symptom monitoring, enhance communication between patients and healthcare providers, and can enable proactive, tailored care (17–19). While widely used in nursing and medical research settings, their application in dietetics remains limited, and no studies to date have examined ePRO-triggered dietetic consultations in early breast and gynaecologic cancer survivorship. By shifting from referral-based to trigger-based models, ePROs may reduce barriers to engagement, respond to patient-centred needs in real time,

support more personalised dietetic interventions, and mitigate gatekeeping of allied health services associated with clinician-mediated referrals.

The Linking You to Support and Advice (LYSA) trial assessed the feasibility and acceptability of delivering personalised support through a dietitian- and nurse-led survivorship intervention in Chapter 3 of this thesis (20). Building on this foundation the present chapter focuses specifically on the dietetic component of the LYSA trial. To our knowledge, this is the first evaluation of a trigger-based, ePRO-initiated dietetic consultation system in early-stage breast and gynaecologic cancer survivors, addressing an important gap in survivorship care.

4.3 AIMS AND OBJECTIVES

The primary aim of this study is to evaluate the feasibility of implementing a trigger-based virtual dietetic consultation system, initiated via ePROs in a cohort of early-stage breast and gynaecologic cancer survivors. Specifically, we aim to determine the proportion of participants who trigger-initiated a dietetic consultation at baseline and at the study endpoint in both arms; identify and characterise the reasons for trigger-initiated dietetic consultations; examine the frequency and patterns of engagement with the dietitian among participants in the experimental arm, who received monthly ePRO surveys between baseline and endpoint.

The secondary aim is to assess changes in body composition and dietary quality from baseline to study endpoint, and to compare these outcomes between the experimental and active comparator arms.

4.4 METHODS AND MATERIALS

4.4.1 Study Design and Setting

This study forms part of the Linking You to Support and Advice (LYSA) Trial, an unblinded randomised controlled trial with an active comparator and experimental arms, conducted across two regional cancer centres in Ireland. The trial assessed the feasibility of a complex nurse and dietitian-led survivorship intervention using ePRO's in early-stage breast and gynaecologic cancer survivors.

The trial protocol, including randomisation procedures, has been published previously (21) and a detailed description of the dietetic-specific intervention protocol is also available in Chapter 2 of this thesis (22). The following section provides a concise summary of the aspects relevant to the present analysis.

4.4.2 Ethical Approval and Trial Registration

The LYSA Trial was retrospectively registered on ClinicaTrials.gov on 5th September 2021 [NCT05035173]. Ethical approval was obtained from the responsible research ethics committees of two Irish cancer centres [CREC Cork Teaching Hospitals ECM 3 08/12/2020; CREC Galway University Hospitals 121/21] and was conducted in accordance with the Declaration of Helsinki and ICH E6 Good Clinical Practice terms.

4.4.3 Participants

Participants invited to enrol in the study included women (assigned female sex at birth) diagnosed with early-stage hormone-receptor positive breast cancer or gynaecologic (cervical, endometrial) cancer. Eligibility criteria included the completion of primary curative therapy within the previous 12 months, and internet access. Written informed consent was obtained via video call or in person at a regional cancer centre by the

research nurse. A detailed overview of the eligibility criteria is available in the primary protocol (21). The sample size (n = 200) was determined to facilitate the feasibility and pilot efficacy objectives, based on the recruitment of the largest possible sample given the funding available and the number of potentially eligible patients during the trial's time frame. As the primary objective of the LYSA Trial was to assess feasibility, the sample size was determined accordingly and was not powered to detect statistically significant treatment effects. Any conclusions regarding secondary outcomes will be hypothesis-generating.

4.4.4 Randomisation and Blinding

The study's principal statistician conducted randomisation, using a 1:1 ratio for breast cancer, cervical cancer and endometrial cancer. Randomisation was conducted using a computer-generated randomisation list via an electronic data capture (Castor Electronic Data Capture [EDC]) (23). The randomisation list used randomly sized blocks of size 4, 6, or 8. Due to the nature of the intervention, the research team were not blinded to the participants' group allocation.

4.4.5 Intervention

Participants enrolled and randomised were invited to complete a baseline and endpoint survey emailed via Castor EDC. The survey included:

- Disease-specific health-related quality of life (HRQoL) assessments using European Organisation for Research and Treatment of Cancer Quality of Life (EORTC QLQ-C30) tool (24) and Patient Reported Outcome Common Terminology Criteria for Adverse Events (PRO-CTCAE) tool (25);
- Body Mass Index;
- Malnutrition Screening Tool (MST) score (26);

- Weight gain concern;
- Fear of recurrence assessment;
- Self-reported physical activity levels using the Nordic Physical Activity Questionnaire (NPAQ)-short questionnaire (27).

Upon survey completion participants were invited to attend the survivorship clinic at a regional cancer centre. Participants in both arms underwent body composition and nutritional assessments at the survivorship clinic. Body composition assessments included weight, height, BMI, waist circumference, handgrip strength, and bioelectrical impedance analysis (BIA). The BIA was conducted using the Fresenius Kabi Body Composition Monitor, which provides manufacturer-derived outputs including lean tissue mass, adipose tissue mass, lean tissue index, and fat tissue index. These outputs are reported using device-specific terminology throughout the thesis and interpreted in relation to established body composition constructs where appropriate. Nutritional assessments included multiple 24-hour dietary recalls (weekend and weekday), World Cancer Research Fund (WCRF) /American Institute for Cancer Research (AICR) food checklist and the European Prospective Investigation into Cancer and Nutrition (EPIC) Norfolk Food Frequency Questionnaire (FFQ). Participants were invited to attend a second survivorship clinic appointment, via a telehealth platform. At the virtual survivorship clinic, participants underwent a second 24-hour recall and completed the FFQ with the research dietitian. The experimental arm underwent cancer-specific dietary education and personalised nutritional counselling, using the WCRF recommendations for survivorship via "Healthy Eating for Cancer Survivors" book (28). The active comparator arm continued to receive routine care with their medical team at regional outpatient oncology clinics.

Participants in the experimental arm were sent a survey every two months over the study period (12 months) that assessed HRQoL, fear of recurrence assessment, BMI, MST score, weight gain concern, and self-reported physical activity status. This survey was transformed into a colour-coded trigger list, prompting a trigger-initiated virtual consultation with the dietitian.

4.4.6 Outcomes

4.4.6.1 Dietetic Consultation Triggers and Decision Pathways

A predefined trigger alert matrix was developed for the experimental arm, specifically relating to dietetic outcomes. For the purpose of this chapter, "symptom triggers" relate to BMI, MST Score and weight gain concern.

Participants triggered if they reported:

- a total MST score of 2 – 7; or
- a BMI of >25.5-29.9kg/m^2 and weight gain concern; or
- a BMI >30kg/m^2.

Reasons for a virtual dietetic consultation during T2 – T10 included symptom trigger; identified nutritional risk by the study nurse; patient requirement; or clinical decision. Participants could trigger a maximum number of five dietetic consultations via symptom surveys. Additional dietetic consultations could be implemented beyond those initiated by a symptom trigger based on clinical decision; patient requirement; or if participants were identified to be at nutritional risk by the study nurse.

Reasons for non-attendance following a symptom trigger initiated dietetic consultation were categorised *a priori* as "no patient answer after 2-3 contacts"; "patient declined – not considered necessary"; "weight inputted incorrectly"; "visit scheduled but patient did not attend"; "trigger overridden by dietitian"; or "other". On occasion,

triggers were overridden at the dietitian's discretion when participants were judged to be progressing satisfactorily with their care plan, despite meeting trigger criteria, in consideration of the limited hours allocated to dietetic support within the trial (20 hours per week). For example, a participant with a BMI >30 kg/m² who had lost 4 kg over two months, had an MST score of 0, and demonstrated increased physical activity may not have been reviewed, as limited dietetic capacity meant that participants judged to be at higher nutritional risk were prioritised.

4.4.6.2 Body Composition

Anthropometric data were collected at baseline and endpoint assessments. Body mass index was calculated using weight (kilograms) and height (centimetres) (29). Waist circumference was taken three times, to the nearest 0.1cm, following the World Health Organisation STEPS Manual (30). An average was used and compared to WCRF Recommendations [Supplementary Table 4.1]. Handgrip strength (HGS) was measured using a Jamar dynamometer. Three measurements were taken on the right and left hand, with an average recorded (31).

Bioelectrical impedance analysis (BIA) was used to measure lean tissue mass, adipose tissue mass, lean tissue index and fat tissue index. Standardised bioelectrical impedance analysis (BIA) procedures were followed in accordance with device manufacturer instructions. Participants received pre-assessment guidance prior to their clinic visit, including avoidance of alcohol for 24 hours, and avoidance of food, caffeine, and strenuous exercise for at least 2 hours prior to measurement. Participants were also instructed not to apply lotions or creams to the hands or feet prior to assessment. Individuals with implanted electronic devices (e.g. pacemakers) or who were pregnant were excluded from BIA measurement.

Prior to measurement, participants were asked to remove shoes, socks, tight clothing, jewellery, and metal objects. Height and weight were measured prior to BIA assessment, after which participants rested in a supine position for approximately 5 minutes before electrode placement. During measurement, participants remained relaxed, in a supine position, with limbs separated to avoid skin-to-skin contact. Electrodes were applied in standardised anatomical positions, and measurements were conducted in a controlled environment to minimise environmental variability.

Lean tissue index (LTI), derived from BIA outputs, was used as an estimate of skeletal muscle mass. A cut-off of <6.75 kg/m² was applied to identify low skeletal muscle mass, based on thresholds reported by Janssen et al. (2004) (32), which were derived from associations with physical disability risk in older adults. These cut-points have been widely used in clinical and epidemiological research as proxies for low muscle mass.

4.4.6.3 Dietary Quality

Dietary quality was assessed using a modified version of WCRF / AICR standardised scoring system (33,34). The scoring system assesses adherence to seven out of ten cancer prevention/survivorship recommendations, including BMI, waist circumference, physical activity, fruit and vegetable intake, fibre consumption, intake of red and processed meats, sugar-sweetened beverages, alcohol consumption, and breastfeeding history. Each component is assigned a score of 1 (recommendation met), 0.5 (partially met), or 0 (not met), yielding a total score ranging from 0 to 7, with higher scores indicating greater adherence to the guidelines. The dietitian calculated these scores using anthropometric measurements, 24-hour dietary recall data, and responses from the FFQ collected at baseline and at 12-month follow-up

[Supplementary Table 4.1]. We excluded the Ultra Processed Foods (NOVA) classification from this trial due to its inconsistent criteria, limited alignment with nutritional evidence, and potential to foster confusion among both experts and the public, as highlighted in critiques of its ambiguity, poor reproducibility, and tendency toward oversimplified or sensationalised interpretations (35–41).

4.4.7 Statistical Analysis

4.4.7.1 Statistical Software and Reporting

All analyses were conducted in R (version 4.5.0; R Foundation for Statistical Computing, Vienna, Austria) using packages including dplyr, tidyr, broom, emmeans, FSA, nnet, and writexl. Continuous variables are reported as means ± standard deviations, and categorical variables as counts and percentages. Adjusted post-intervention means, least-squares mean differences, 95% confidence intervals, and p-values were reported where applicable.

4.4.7.2 Dietetic Consultation Triggers and Decision Pathways

The dataset was transformed to generate several derived variables. A binary variable was created to indicate whether each experimental arm participant ever triggered a dietetic alert across the intervention period (T2–T10), and in all arms at baseline (T0) and endpoint (T12). Separate binary variables were generated for each type of trigger (MST-initiated, BMI, weight gain concern). Records in which non-attendance was documented as "Trigger Overridden by Dietitian" were removed prior to analysis to avoid misclassification of dietitian-cancelled visits as patient non-attendance. The total number of attended virtual consultations was calculated for each participant from T2-T10. In the experimental arm, instances of non-attendance following a triggered consultation were tallied, and reasons were categorised according to predefined codes.

For participants who triggered at least once, the proportion of trigger-related consultations attended was computed to assess engagement with the intervention. Additionally, reasons for all completed consultations, whether due to nutritional risk, symptom trigger, participant request, or clinical judgement, were recorded and categorised to support stratified analyses of visit purpose.

4.4.7.3 Body Composition

Body composition parameters (weight, BMI, waist circumference, lean body mass, lean tissue index, fat tissue index, adipose tissue mass) and HGS centiles were summarised at baseline and post-intervention by study arm. Baseline comparisons between arms were performed using independent t-tests, and post-intervention differences were estimated using ANCOVA, adjusting for baseline values. Within-arm changes in HGS centiles were categorised as 'Up,' 'Down,' or 'No change' based on numeric coding of baseline and endpoint centile categories (1-6), with counts and percentages of each movement category summarised, and changes from T0 and T12 evaluated using Wilcoxon signed-rank tests when parametric assumptions were not met. Associations between changes in body composition and intervention engagement or patient-reported outcomes were assessed using correlation and linear regression analyses within the experimental arm. Post-hoc analyses included Dunn's tests for significant Kruskal-Wallis comparisons and Bonferroni-corrected pairwise comparisons for categorical outcomes.

4.4.7.4 Dietary Quality

Changes in dietary quality from baseline (T0) to post-intervention (T12) were assessed within the experimental and comparator arms using paired t-tests or Wilcoxon signed-rank tests, and between-arm differences were evaluated using independent t-tests or

Mann-Whitney U tests. WCRF adherence was scored per recommendation (0 = not met, 0.5 = partially met, 1.0 = fully met), with total scores summed across recommendations. Associations between adherence to dietetic counselling and post-intervention WCRF scores were explored using correlation and linear regression analyses within the experimental arm. Significant subgroup differences or associations were further examined with post-hoc analyses. Statistical significance was interpreted using two-sided p-values of < 0.05 or < 0.01.

4.4.7.5 Group Comparisons and Regression Analyses

Associations between engagement with dietetic intervention, trigger-initiated consultations and participant characteristics were evaluated using the following approaches. For categorical variables (e.g. menopause status, economic status, education), Kruskal-Wallis tests were performed, with significant results further examined using post-hoc Dunn's pairwise comparisons and Benjamini-Hochberg correction; unadjusted p-values were also reported to identify trends. For numeric predictors (e.g. days since treatment end, EORTC baseline scores) Spearman's rank correlations were calculated. Count outcomes were modelled using Poisson or Negative Binomial regression to account for overdispersion, with regression coefficients exponentiated to provide incidence rate ratios (IRRs) and 95% confidence intervals. Results were interpreted using both effect sizes and statistical significance thresholds

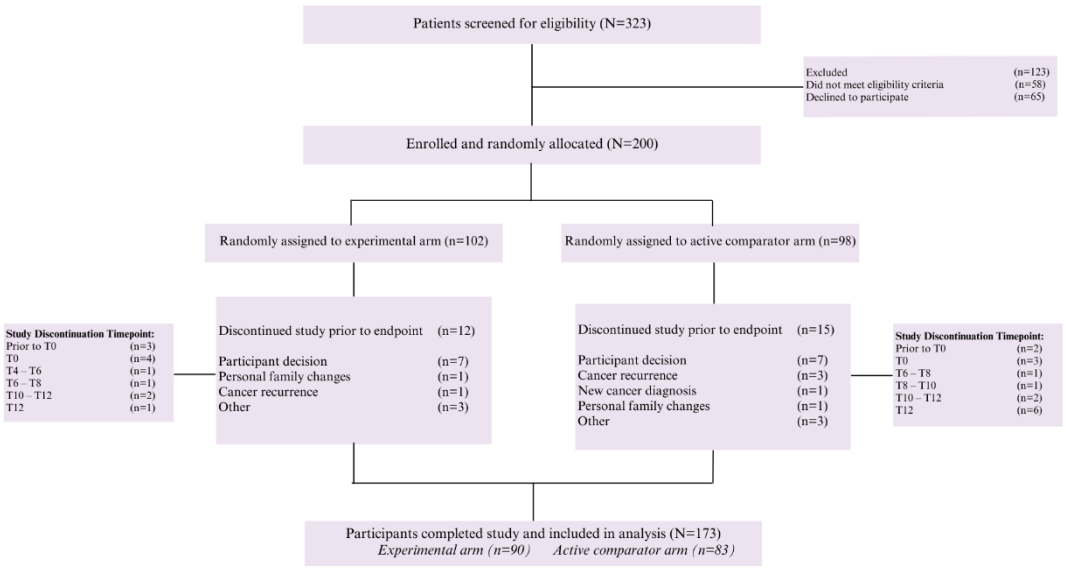


Figure 4.1: CONSORT Diagram

4.5 RESULTS

4.5.1 Participant Characteristics

Of 325 patients screened, 200 participants were enrolled. Following randomisation, 102 participants were assigned the experimental arm and 98 to the active comparator arm. A total of 173 (n = 86.5%) participants completed the trial [Figure 4.1].

Reasons for study discontinuation included participant decision (n = 18), cancer recurrence (n = 4), new cancer diagnosis (n = 1) and other (n = 4).

The mean age was 55.2 ±10.5 years and breast cancer accounted for 84% of the cohort (Table 4.1). The majority of participants had completed third level education and were enrolled between 6 months and 1-year post-diagnosis.

Table 4.1: Baseline Clinicopathologic and Sociodemographic Characteristics

Baseline Clinicopathologic and Sociodemographic Characteristics		**Experimental Arm (n = 102)** *n (%)*	**Active Comparator Arm (n = 98)** *n (%)*	**P value**
Age (years), ***Mean, Standard Deviation***		54.96 (10.33)	55.45 (10.72)	0.746
Age Group	20-24	1 (1.0)	0 (0.0)	0.621
	30-34	2 (2.0)	2 (2.0)	
	35-39	2 (2.0)	5 (5.1)	
	40-44	9 (8.8)	10 (10.2)	
	45-49	12 (11.8)	15 (15.3)	
	50-54	26 (25.5)	14 (14.3)	
	55-59	14 (13.7)	14 (14.3)	
	60-64	10 (9.8)	15 (15.3)	
	65-69	13 (12.7)	9 (9.2)	
	70-74	7 (6.9)	9 (9.2)	
	75-79	1 (1.0)	2 (2.0)	
Primary Tumour Location	Breast	84 (82.4)	84 (85.7)	0.807
	Cervical	8 (7.8)	6 (6.1)	
	Endometrial	10 (9.8)	8 (8.2)	
Time from Diagnosis to Study Entry	Between 6 months and 1 year	56 (54.9)	53 (54.1)	0.969
	Less than 6 months	24 (23.5)	23 (23.5)	
	More than 1 year up to 2 years	19 (18.6)	20 (20.4)	
Time from End of Treatment to Study Entry (months)	0 – 2 months	59 (57.8)	56 (57.1)	0.379
	2 – 4 months	17 (16.7)	12 (12.2)	
	4 – 6 months	5 (4.9)	4 (4.1)	
	6 – 8 months	5 (4.9)	3 (3.1)	
	8 – 10 months	3 (2.9)	10 (10.2)	
	10 – 12 months	7 (6.9)	9 (9.2)	
	>12 months	0 (0.0)	1 (1.0)	
Menopausal Status	Peri	13 (12.7)	7 (7.1)	0.166
	Post	53 (52.0)	57 (58.2)	
	Pre	33 (32.4)	28 (28.6)	
	Unknown	0 (0.0)	4 (4.1)	
Previous Surgery	No	4 (3.9)	5 (5.1)	0.853
	Yes	95 (93.1)	91 (92.9)	
Previous Chemotherapy	No	36 (35.3)	39 (39.8)	0.632
	Yes	62 (60.8)	57 (58.2)	
Previous Radiotherapy	No	1 (1.0)	2 (2.0)	0.765
	Yes	98 (96.1)	94 (95.9)	
Current Endocrine Therapy Regimen	Anastrozole	35 (34.3)	36 (36.7)	0.817

	Anastrozole/goserelin	4 (3.9)	4 (4.1)	
	Exemestane	3 (2.9)	5 (5.1)	
	Exemestane/goserelin	2 (2.0)	1 (1.0)	
	Letrozole	7 (6.9)	4 (4.1)	
	Tamoxifen	27 (26.5)	32 (32.7)	
	Tamoxifen/goserelin	2 (2.0)	1 (1.0)	
Body Mass Index (kg/m^2) *MEAN, STANDARD DEVIATION*		29.37 (5.98)	27.66 (7.23)	0.078
Ethnicity	White Irish	91 (89.2)	86 (87.8)	0.646
	Any other white background	6 (5.9)	8 (8.2)	
	Any other Asian background	1 (1.0)	0 (0.0)	
	Chinese	0 (0.0)	1 (1.0)	
Education Level	None at all	1 (1.0)	0 (0.0)	0.844
	Primary level	3 (2.9)	2 (2.0)	
	Secondary level	30 (29.4)	32 (32.7)	
	Third level (college/university)	64 (62.7)	61 (62.2)	
Economic Certainty	Coping on present income	44 (43.1)	38 (38.8)	0.648
	Living comfortably on present income	33 (32.4)	40 (40.8)	
	Difficult on present income	13 (12.7)	11 (11.2)	
	Very difficult on present income	6 (5.9)	6 (6.1)	
	Rather not say	2 (2.0)	0 (0.0)	
Economic Status	Unable to work due to sickness or disability	33 (32.4)	35 (35.7)	0.859
	Employed	31 (30.4)	26 (26.5)	
	Retired	17 (16.7)	17 (17.3)	
	Looking after home/family	11 (10.8)	8 (8.2)	
	Student	2 (2.0)	1 (1.0)	
	Unable to work due to COVID restrictions	1 (1.0)	0 (0.0)	
	Unemployed, looking for a job	1 (1.0)	3 (3.1)	
	Unemployed, not looking for a job	1 (1.0)	2 (2.0)	
	Other reasons	1 (1.0)	3 (3.1)	
Total EORTC Score *Mean, Standard Deviation*		60.42 (12.54)	58.15 (11.43)	0.190

Abbreviations: EORTC, European Organisation for Research and Treatment of Cancer

4.5.2 Dietetic Consultation Triggers and Decision Pathways

MST triggers were uncommon (<10%) at baseline (active comparator 9.6% [n = 8]; experimental 8.9% [n = 8]) and decreased slightly by endpoint (4.8% [n = 4]; 5.6% [n = 5]; Figure 4.2). In the experimental arm (n = 90), MST triggers fell from 7.8% (T2) to 3.3% (T10). The highest MST score at both baseline and endpoint was 4, observed exclusively in participants from the active comparator arm.

BMI triggers were more common than MST triggers. At baseline, 47% of participants (n = 39) in the active comparator arm and 60% (n = 54) in the experimental arm experienced BMI triggers. These rates were similar at endpoint: 48.2% (n = 40) in the active comparator arm and 60% (n = 54) in the experimental arm (Figure 4.3). Looking specifically at the experimental arm over time (n = 90), BMI triggers decreased at T4 and T6 compared with higher rates observed at T2 and again at T10.

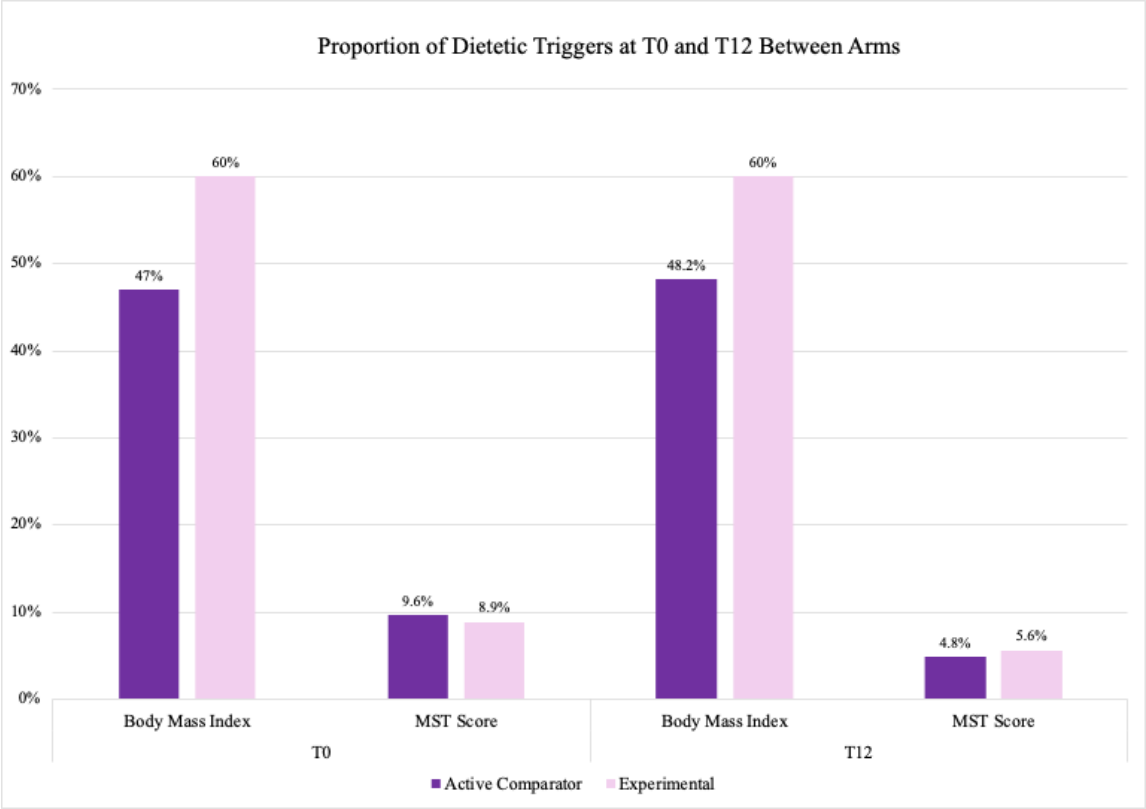


Figure 4.2: Proportion of Dietetic Triggers at T0 and T12 between arms

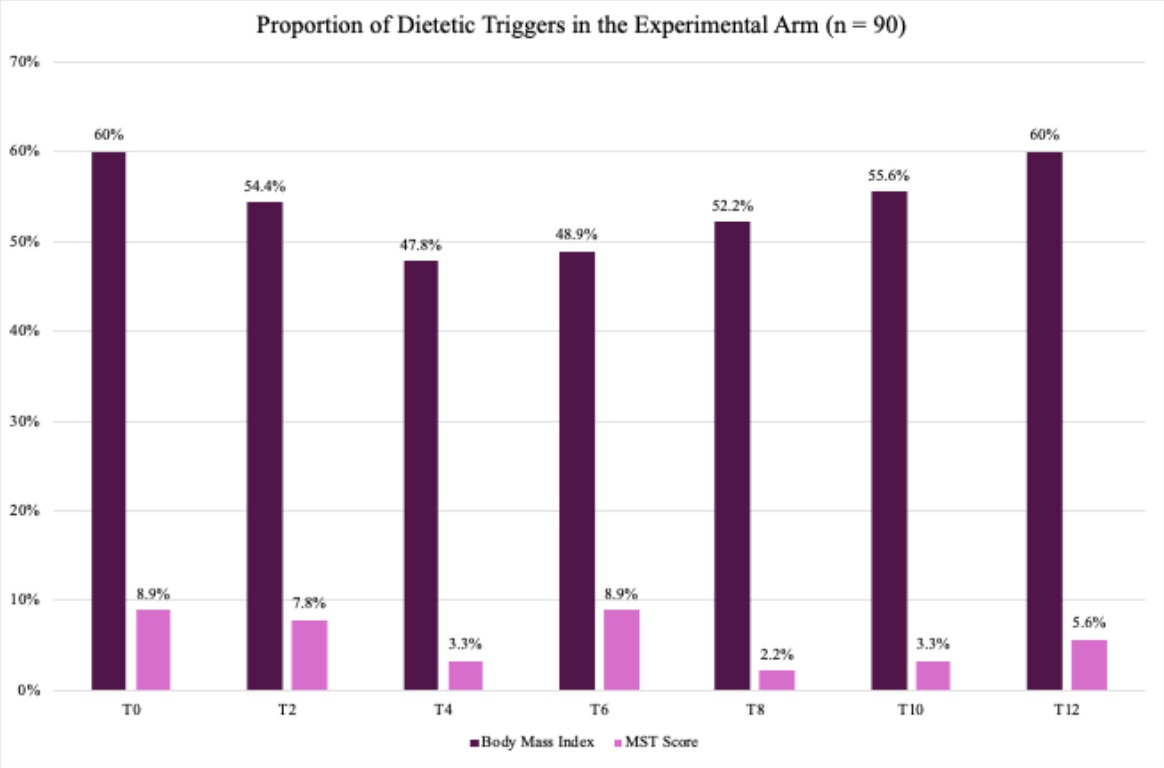


Figure 4.3: Proportion of Dietetic Triggers in the Experimental Arm

4.5.2.1 Trigger-Initiated Dietetic Consultations in the Experimental Arm

In the experimental arm, the main reason for virtual dietetic consultations were due to symptom triggers (n = 256, 76.6%), followed by clinical decision (n = 61, 18.3%), patient requirement (n = 14, 4.2%) and lastly, identified nutritional risk (n = 3, 0.9%).

In the experimental arm, 40.5% (n = 36) of participants trigger-initiated five dietetic consultations over the intervention period, whilst 23.6% (n = 21) did not trigger at all. Approximately one quarter of participants (24.7%) trigger-initiated between one to two dietetic consultations, whilst 11.2% trigger-initiated three to four dietetic consultations. Over the intervention period, additional dietetic consultations were conducted due to patient requirement, clinical decision or identified nutritional risk (n = 14). The number of additional visits for participants, outside of those initiated by a trigger, ranged from one (n = 5) to five (n = 2).

Overall, 27.8% (n = 93) of dietetic consultations were not attended, excluding those who had a trigger overridden by a dietitian. The main reasons were "*Other*" (46%), "*Patient declined – not considered necessary*" (26.9%), and "*No patient answered after 2-3 contacts within a week*" (14%). Scheduled visits not attended accounted for 8.6% and incorrectly reported weights (stones/pounds instead of kilograms) falsely triggering consultations accounted for 4.3%.

"*Other*" reasons included participants not answering at first contact, with the dietitian requesting a call back (37.2%); the participant answering but reporting they were unable to speak with the dietitian (20.9%); the participant having a review in between symptom surveys, with an additional appointment not considered necessary (14%); dietetic input classed as inappropriate due to other medical illness or incident reported by the participant themselves or by a healthcare professional (11.6%); participants not attending a full consultation with only a short review being completed (7%); participants requested an appointment at another timeframe (e.g. 1 month) (7%); or a consultation for a non-cancer related dietetic intervention with a referral back to the primary care physician (2.3%).

Of participants who initiated a dietetic consultation, for any reason, 42% attended all scheduled consultations, 19.3% attended 60% - 80%, and 8% of participants attended 0 - 20%. Trigger-initiated consultations (T2 – T10) required 57.8 hours of dietetic services, with the median length of consultations 40 minutes (IQR 30 – 75). Assessment consultations in both arms at T0 and T12 were longer, with a median length of 90 minutes (IQR 70 – 120).

Identified nutritional risk was higher among participants unable to work due to COVID or caring for home/family compared with employed participants ($p = 0.045$).

Lower economic certainty was associated with higher clinical decision trigger counts (*p = 0.0076*) and patient requirement trigger counts (*p = 0.0038*), while higher patient requirement trigger counts were positively associated with baseline EORTC total scores (*rho = 0.254, p = 0.018*). Trends were observed between patient requirement trigger counts and age-adjusted left handgrip centiles (*p = 0.047*), though pairwise comparisons were not significant after adjustment.

Non-attendance varied by reason and was associated with participant characteristics. For non-attendance due to no response following 2-3 contacts within a week, associations were observed with age group (*p = 0.023*), economic status (*adjusted p = 0.017 - 0.034*), and economic certainty (*adjusted p = 0.034 - 0.046*). Participants unable to work due to COVID restrictions or unemployed, and those selecting "Rather not say" for economic certainty, had higher non-attendance. For non-attendance due to participants not attending a scheduled visit, economic certainty was associated (*p = 0.017*) with trends toward higher non-attendance among participants reporting "difficult" or "very difficult" income, although no pairwise comparisons remained significant after adjustment.

4.5.3 Body Composition

At baseline, mean body weight was similar between the experimental (78.4 ± 17.6 kg) and comparator arms (75.6 ± 19.2 kg), as were waist circumference, lean tissue mass, and adipose tissue mass (Table 4.2). At endpoint, no significant between-group differences were observed for body weight, BMI, waist circumference, lean or fat tissue indices, adipose mass, or handgrip strength (all *p > 0.24*) (Table 4.2). The adjusted differences in means (experimental minus active comparator) were small and

statistically non-significant, with 95% confidence intervals crossing zero for all variables.

Table 4.2: Body Composition Changes Between Arms with Estimated Treatment Effects

Body Composition Characteristics	Study Arm at Baseline *(Mean [SD])*		Study Arm at Endpoint *(Mean [SD])*		P value *	Difference in Means [95% Confidence Intervals] (Experimental – Active Comparator)
	Active Comparator *(n = 83)*	Experimental *(n = 90)*	Active Comparator *(n = 83)*	Experimental *(n = 90)*		
Body Weight (kg)	75.6 ± 19.2	78.4 ± 17.6	76.2 ± 19.5	78.4 ± 18.3	0.521	-0.41 [-1.67 to 0.85]
BMI (kg/m^2)	27.8 ± 7.5	29.3 ± 5.9	28.1 ± 7.7	29.2 ± 6	0.327	-0.23 [-0.70 to 0.23]
Waist Circumference (cm)	94.3 ± 15.4	96.7 ± 18.4	93.4 ± 16.1	96 ± 14.7	0.431	0.89 [-1.34 to 3.13]
Lean Tissue Mass (kg)	33.5 ± 5.9	34.2 ± 7.5	33.5 ± 15.6	36.1 ± 7	0.286	1.80 [-1.52 to 5.13]
Lean Tissue Index (kg/m^2)	12.4 ± 2	12.8 ± 2.4	11.7 ± 12.2	13.4 ± 2.1	0.244	1.54 [-1.06 to 4.14]
Fat Tissue Index (kg/m^2)	15.5 ± 7.6	16.1 ± 6.5	14.1 ± 14.4	15.7 ± 6.4	0.327	1.19 [-1.20 to 3.58]
Adipose Tissue Mass (kg)	41.8 ± 20.9	42.6 ± 17.8	39.4 ± 25.4	41.7 ± 17.8	0.216	1.93 [-1.14 to 4.99]
Handgrip Strength (kg)	22.56 ± 14.31	24.24 ± 6.71	23.02 ± 5.33	24.11 ± 6.89	0.394	0.74 [-0.98 to 2.47]

* P value for estimated treatment effects between arms at study endpoint (12 months)

Abbreviations: BMI; Body Mass Index, SD, standard deviation

Body weight remained stable across both arms (*difference in means: -0.41 kg; [95% CI -1.67 to 0.85]*), as did BMI (*-0.23 kg/m²; [95% CI -0.70 to 0.23]*) and waist circumference (*0.89 cm; [95% CI -1.34 to 3.13]*). Sarcopenia was not identified in any arm at baseline or endpoint, with lean tissue index remaining non-significant between arms (*difference in means: 1.54kg/m^2; [95% CI -1.06 to 4.14]).* In an exploratory analysis, a longer time since treatment completion was associated with a small but statistically significant increase in lean tissue mass change at endpoint in the experimental arm (*coefficient = 0.0105, p = 0.035; R^2: 0.051*).

Age-adjusted handgrip strength centiles were examined to assess functional changes over the intervention period, allowing comparison of shifts in relative strength between arms. At baseline, 17.9% (n = 33) of all randomised participants had a grip-

strength that was lower than the 10th centile for their age, whilst 28.3% (n = 52) had a grip strength between the 10th – 25th centile. Only 3.3% (n = 6) recorded a grip strength that was greater than the 90th centile for their age. At endpoint, 58% (n = 51) of participants in the experimental arm maintained their grip strength centile compared to 52.5% (n = 42) in the active comparator arm. Similar proportions in both arms increased their grip strength centile, 19.3% (n = 17) and 18.8% (n = 15) in the experimental and active comparator arms, respectively. In the active comparator arm, 28.8% (n = 23) experienced a decrease in handgrip centile over 12 months, compared to 22.7% (n = 20) in the experimental arm.

Patient-reported weight gain concern was evaluated at baseline and endpoint in both arms to explore whether perceived changes in body composition differed between arms (Table 4.3). At endpoint, the proportion of participants reporting weight gain concern decreased significantly from baseline in the experimental arm to 46.7% (n = 42) compared with 68.7% in the active comparator arm ($p = 0.01$)

Each additional year of age significantly reduced the odds of reporting weight gain concern by 5% ($OR = 0.95$, $p = 0.002$). Participants who had undergone surgery (62.0% vs 12.5%, $p = 0.003$) and those receiving combination endocrine therapy with goserelin ($p = 0.03$) were more likely to report weight gain concern. In the experimental arm, a higher number of symptom triggers was associated with an increased odds of reporting weight gain concern at endpoint ("Unsure" ($p = 0.046$) and "Yes" ($p = 0.006$).

Table 4.3: Difference in Patient Reported Weight Gain Concern at T0 and T12 between arms

Patient Reported Weight Gain Concern	Study Arm at Baseline N (%)		Study Arm at Endpoint N (%)		P value *
	Experimental (n = 90)	Active Comparator (n = 83)	Experimental (n = 90)	Active Comparator (n = 83)	
Yes	53 *(58.9%)*	52 *(62.7%)*	42 *(46.7%)*	57 *(68.7%)*	**0.012**
Unsure	4 *(4.4%)*	8 *(9.6%)*	6 *(6.6%)*	9 *(10.8%)*	0.275
No	33 *(36.7%)*	23 *(27.7%)*	42 *(46.7%)*	17 *(20.5%)*	**< 0.001**

* P value for estimated treatment effects between arms at study endpoint (12 months)

4.5.4 Dietary Quality

At baseline, WCRF/AICR dietary quality scores were similar between study arms, where higher scores reflect higher adherence to the recommendations. Mean total scores were 3.27 ± 1.28 in the experimental arm and 3.52 ± 1.27 in the active comparator arm, meeting only approximately 50% of the total adherence scores. Component scores for BMI, waist circumference, physical activity, fruit and vegetable intake, fibre, red and processed meat, sugar-sweetened beverages, ethanol and breastfeeding were comparable between arms (Table 4.4).

At endpoint, there were statistically significant differences between study arms in adherence scores for red and processed meat (experimental 0.56 ± 0.35 vs. active comparator 0.45 ± 0.40; *p = 0.030, adjusted difference 0.12 [95% CIs 0.012 - 0.229]*) and sugar-sweetened beverages (*experimental 0.81 ± 0.26 vs. active comparator 0.74 ± 0.26; p = 0.041, adjusted difference 0.077 [95% CIs 0.003 - 0.15]*). There was a significant difference in physical activity adherence scores between study arms, with lower scores in the experimental arm (0.32 ± 0.40) compared with the active comparator arm *(0.44 ± 0.41; p = 0.041, adjusted difference -0.12 [95% CIs -0.238 to 0.005]*). Adherence to fruit and vegetable recommendations was slightly higher in the experimental arm (0.24 ± 0.17) than in the active comparator arm (0.19 ± 0.17), though this difference did not reach statistical significance (*p = 0.079; adjusted difference*

0.043 [95% CIs -0.005 to 0.091]). Total adherence scores decreased in both arms by 12 months: 3.13 ± 1.70 in the experimental arm and 3.02 ± 1.66 in the active comparator arm, with no significant between arm difference (*p = 0.513; adjusted difference 0.115 [95% CIs -0.231 to 0.461]*).

Table 4.4: WCRF/AICR Dietary Quality Score Adherence between Arms at T0 and T12 with Estimated Treatment Effects

Recommendation	Study Arms at Baseline (Mean [SD])		Study Arm at Endpoint (Mean [SD])		P value *	Adjusted Mean Difference (Experimental – Active Comparator) [95% Confidence Intervals]
	Experimental Arm (n=90)	Active Comparator Arm (n = 83)	Experimental Arm (n=90)	Active Comparator Arm (n = 83)		
BMI	0.21 ± 0.21	0.27 ± 0.20	0.22 ± 0.20	0.23 ± 0.20	0.064	0.045 [-0.003 to 0.093]
Waist Circumference	0.10 ± 0.17	0.14 ± 0.19	0.14 ± 0.20	0.14 ± 0.20	0.089	0.026 [-0.004 to 0.055]
Physical Activity	0.33 ± 0.38	0.34 ± 0.40	0.32 ± 0.40	0.44 ± 0.41	**0.041**	-0.122 [-0.238 to 0.005]
Fruit and Vegetables	0.27 ± 0.18	0.26 ± 0.17	0.24 ± 0.17	0.19 ± 0.17	0.079	0.043 [-0.005 to 0.091]
Fibre	0.35 ± 0.13	0.33 ± 0.14	0.34 ± 0.14	0.33 ± 0.15	0.705	0.008 [-0.036 to 0.053]
Red and Processed Meat	0.41 ± 0.37	0.40 ± 0.39	0.56 ± 0.35	0.45 ± 0.40	**0.030**	0.120 [0.012 to 0.229]
Sugar Sweetened Beverages	0.68 ± 0.36	0.73 ± 0.33	0.81 ± 0.26	0.74 ± 0.26	**0.041**	0.077 [0.003 to 0.150]
Ethanol	0.76 ± 0.35	0.81 ± 0.31	0.72 ± 0.34	0.69 ± 0.34	0.353	0.049 [-0.056 to 0.154]
Breastfeeding ~	0.41 ± 0.44	0.44 ± 0.44	0.41 ± 0.44	0.46 ± 0.44		
Total Score	3.27 ± 1.28	3.52 ± 1.27	3.13 ± 1.70	3.02 ± 1.66	0.513	0.115 [-0.231 to 0.461]

* P value for estimated treatment effects between arms at study endpoint (12 months)

~ No p value of adjusted mean difference reported for estimated treatment effects at study endpoint as it was not a modifiable factor within the intervention

In the experimental arm (n = 90), adherence scores showed significant changes over 12 months. Red and processed meat adherence scores increased from an adjusted mean of 0.393 at baseline to 0.565 at 12 months *(+0.172, p < 0.0001*), and sugar-sweetened beverages adherence scores increased from 0.689 to 0.806 *(+0.117, p < 0.0001*). Fruit

and vegetable adherence decreased from 0.272 to 0.235 *(-0.037, $p = 0.0351$)*, and waist circumference adherence decreased from 0.206 to 0.136 *(-0.070, $p < 0.0001$)*. No significant changes were observed for BMI, physical activity, fibre, ethanol, or total score.

Total trigger count was negatively correlated with WCRF dietary quality adherence (*r = -0.364 to -0.532, $p < 0.001$*), indicating that higher adherence was associated with fewer reported triggers. There were no other statistically significant associations reported.

4.6 DISCUSSION

In this randomised controlled trial, a trigger-based, ePRO-initiated dietetic intervention was feasible and well-accepted by early-stage breast and gynaecologic cancer survivors, with good engagement and attendance, and reductions in patient-reported weight gain concern despite minimal changes in body composition or dietary quality. The retention rate was high, with 86.5% of participants completing the trial and most dietetic consultations were initiated in response to symptom triggers (76.6%), supporting the practicality of this model. Consistent with the literature, the use of ePROs in cancer survivorship appears both feasible and acceptable, improving quality of life, enhancing communication between clinicians and clients and facilitating efficient clinical encounters (19,42). There is a lack of evidence of the use of ePROs in chronic disease management (43). However these findings suggest potential for expanding traditional nurse and medical led ePROs to diverse clinical settings (42).

The distribution of symptom and anthropometry-based triggers not only demonstrates the feasibility of an automated dietetic consultation pathway but also

reveal important gaps in how nutritional risk is perceived and acted upon in early-stage breast and gynaecologic cancer survivors. Attendance behaviour suggested generally positive engagement with dietetic support; however, perceived need strongly influenced non-participation. Many declined consultations because they did not view them as necessary, underscoring an ongoing challenge in aligning automated symptom triggers with patient-perceived relevance and readiness to engage. Engagement was limited in some instances by participants' lack of awareness that they had initiated a trigger, resulting in unanticipated dietetic follow-up.

These attendance patterns also highlight significant system-level constraints. Delivering the intervention required substantial resource input, with the study dietitian employed for only 20 hours per week, assuming clinical, administrative, and data-management responsibilities. Limited capacity occasionally necessitated clinical judgement to override automated triggers, illustrating how staffing shortages can directly shape intervention fidelity and potentially moderate effectiveness. These findings mirror broader challenges within the Irish health service, where insufficient dietetic staffing and administrative support hinder the scalable implementation of survivorship services; currently, there is estimated to be just one dietitian for every 4,500 oncology patients (44)**.** Consistent with recent recommendations by Ryding et al. (2025) (16) formally quantifying dietetic time and workload demands will be critical to inform future cost-effectiveness assessments and the development of sustainable, resource-efficient models of care.

Patterns of nutritional risk identification revealed important limitations in the triggering system. While BMI-based criteria captured the majority of participants at

both timepoints, the MST identified very few individuals, suggesting that key aspects of nutritional risk may go undetected when relying solely on malnutrition-based screening. Within the experimental arm, most participants did engage with dietetic support when prompted, and nearly one-quarter did not trigger throughout the intervention period, suggesting that they did not require dietetic input based on the pre-defined triggers. However, an important consideration is that the BMI trigger did not account for weight gain among those within the healthy BMI range, and therefore the system may have overlooked a clinically important trajectory, potentially influencing weight-related outcomes. Malnutrition is frequently associated with haematologic, lung, genitourinary and uterine tumours, with rates generally lower in colorectal and breast cancers (45). Furthermore, sarcopenia was not identified in this cohort using thresholds from Janseen et al. (2004) (32). In a systematic review, Aleixo et al. (2019) highlighted that bioelectrical impedance analysis is an accurate method for detecting sarcopenia in adults with cancer prior to treatment, with varying thresholds (46), However Prado et al. (2018) identified the performance of BIA in outpatient populations as poor in diagnostic performance, referring to the availability of cut off values; moderate in the accuracy of techniques and costs; and sufficient in test-retest reliability and follow-up feasibility (47). Further research needs to be conducted in assessing the diagnostic performance of BIA in breast and gynaecologic cancer survivors, and how this can be utilised as an effective diagnostic tool. In recent literature, breast cancer survivors were least likely to have dietetic consultation despite being the cohort who desired it the most (15). More consideration should be given to the symptoms experienced by this cohort that may have an indirect effect on dietary patterns, such as vasomotor symptoms (48), insomnia, fatigue (49), and disordered eating behaviours (50). Currently, standard dietetic screening tools do not capture nor

consider patient reported symptoms in this way. Given this, and the identification rates of malnutrition in the LYSA cohort, there is a need for a multi-dimensional nutritional assessment tool that fully encapsulates all treatment and tumour-related symptoms that may impact nutritional intake and dietary behaviours.

Trujilo et al. (2024) systematically reviewed validated nutritional screening tools in adult oncology outpatient settings and identified six validated screening tools, including the MST, Mini Nutritional Assessment (MNA), NUTRISCORE, Nutrition Risk Screening-2002, and the Patient Generated Subjective Global Assessment (PG-SGA) (51). Although tools such as the PG-SGA capture nutrition impact symptoms traditionally linked to malnutrition, none are designed to identify individuals experiencing or at risk of treatment-related weight gain as requiring nutritional intervention. This gap is particularly important given the broader nutritional challenges faced by this cohort, including iatrogenic menopause and its metabolic consequences, elevated risks of osteoporosis and cardiovascular disease, the risk of disordered eating patterns, and complex decisions around supplement use. This further underscores the need for screening approaches that extend beyond undernutrition to capture the full spectrum of nutritional risk in survivorship. For example, incorporating a BMI-based trigger initiating dietetic consultation following a two standard deviation increase may more effectively identify individuals whose nutritional needs and chronic disease risk are driven by treatment-related weight gain rather than weight loss.

Another important consideration in interpreting these results is that participants also received an intervention from a nurse, which addressed 23 additional symptom triggers using validated tools, such as *PRO-CTCAE* and *EORTC-C30* assessments. The dual nature of the intervention, delivered within the same timeframe, may have

introduced an unmanageable degree of behavioural and cognitive complexity for some participants – a challenge frequently reported in survivorship literature (52,53). Cancer survivors often navigate substantial symptom burden, including fatigue, vasomotor symptoms, sleep disturbances and gastrointestinal changes, all of which can impair capacity to engage in multiple simultaneous behaviour change tasks (52,53). Evidence from digital and clinician-supported survivorship interventions shows that adherence declines when patients are asked to manage parallel goals or self-monitoring requirements, particularly when symptoms are prominent or fluctuating (54). Furthermore, Jayeoba et al. (2025) found that oncologists preferred low-burden, electronic health record-integrated tools to reinforce behaviour-change goals and that, without such integration, both clinicians and patients struggled to maintain long-term engagement (55).

Weight management adds an additional layer of complexity: metabolic alterations associated with endocrine therapy, iatrogenic menopause, emotional distress, and reduced physical functioning create a uniquely challenging environment for sustained dietary change. Literature from Perperidi et al. (2023), Shen et al. (2024) and Zhang et al. (2025) report that nutritional counselling can be effective, but only when the intervention intensity is carefully paced and aligned with symptom load (56–58).

These findings highlight limitations of existing screening tools in capturing treatment- and symptom-specific nutritional needs, including risk of weight gain. They emphasise the need for a multidimensional, survivorship-specific tool that identifies participants who would benefit from dietetic intervention. Given the high engagement with the ePRO system future research should refine symptom triggers and integrate them with multidisciplinary assessments, investigating the effects of parallel interventions and potential synergistic effects of multidisciplinary teams in this cohort.

Building on these insights, it is important to consider how the intervention influenced body composition and dietary quality, highlighting the relationship between personalised nutrition support, symptom burden, and adherence to recommended dietary patterns. Body weight and BMI remained stable over the intervention period in the experimental arm, with only small, non-significant increases in lean tissue mass. According to the American Cancer Society guidelines while lifestyle interventions are recognised as beneficial, short-term nutritional interventions may show minimal changes in body composition (6). For example, Reeves et al. (2021) reported a 4.5% weight loss over 12 months in breast cancer survivors receiving intensive counselling (n = 22 contacts in 12 months) and a low-calorie diet (*[95% CIs -6.5 to -2.5], $p < 0.001$*) compared with controls (59). Similarly, Braun et al. (2018) demonstrated positive weight loss with weekly remote counselling, practical demonstrations, and group education over six months in predominantly breast cancer survivors (60). In contrast, LYSA was not a weight loss intervention; its primary outcome was to assess feasibility and acceptability of a complex survivorship intervention. Body mass index was not an exclusion criterion in this trial, meaning that participants had a range of dietetic goals and not a focus on calorie deficits. These factors likely contributed to the minimal changes observed in body composition compared with other nutritional interventions focussed on weight loss.

Despite stable body weight, participants reported a significant reduction in weight gain concern over the intervention period. This highlights the value of dietetic input in shaping perceptions of weight management and reducing weight-related stigma, independent of actual changes in body composition and the complexity of delivering personalised nutritional counselling, which contrasts with international oncology guidelines that simply advise patients to "*avoid being overweight*" during survivorship

(61). Furthermore, these findings suggest that dietetic interventions, when delivered with appropriate counselling techniques, may play an important role in reducing weight-related stigma following a cancer diagnosis, positively influencing participants' perceptions and confidence regarding weight management, independent of actual changes in body composition. Notably, participants experiencing higher symptom burden may have engaged less with diet-related behaviours despite attending dietetic consultations, highlighting the need for symptom-specific targeting in future interventions (52,53).

Adherence to WCRF scores showed small but non-significant differences in means between the experimental and active comparator arms. Baseline dietary quality scores in this cohort were lower than that of European counterparts, for example, the Nutri-Net Santé cohort (n = 41,543) reported an average WCRF score of 4.8 ±1.1 (62). While WCRF/AICR scores are associated with cancer risk, they do not account for treatment-specific symptoms that may restrict dietary intake, such as post-pelvic radiation–related gastrointestinal symptoms warranting reduced fibre or fruit and vegetable intake (63). This prescribed dietary therapy will result in lower WCRF adherence independent of dietary effort and important symptom management. Participants with fewer symptom triggers demonstrated higher adherence to WCRF recommendations ($p = 0.00046$), suggesting the score may not accurately reflect nutritional considerations in this cohort. Although differences in WCRF adherence were small, the clinical significance for long-term cancer or chronic disease outcomes remains uncertain, reflecting limitations of existing nutritional screening tools in oncology survivorship (51) and evidence that adherence declines when patients must manage multiple goals amid symptom burden (55). Given the exclusion of ultra-processed food recommendations and the absence of tumour- or symptom-specific

considerations, alternative scoring approaches, such as a Mediterranean Dietary Quality score, may better capture dietary quality in survivorship. The European Society of Menopause and Andropause (EMAS) highlights the role of a Mediterranean-style diet in managing menopausal symptoms (64), which is particularly relevant for HR+ breast and gynaecologic cancer survivors. Fatigue and cognitive decline, common in this population, may also impact diet adherence (65–67), with evidence supporting positive effects of the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet on cognition and memory (68).

The personalised, rather than standardised, counselling approach is an important consideration. Tailoring advice to participants' knowledge, behaviour, readiness for change, and individual circumstances likely enhanced engagement (56–58). Consistent with evidence from digital and clinician-supported interventions, engagement is maximised when dietary counselling is tailored to participant readiness and symptom load rather than delivered in parallel with multiple competing goals (55). Shifting from a weight-centred to a dietary behaviour–centred approach may also reduce pressure and stigma experienced by survivors, support long-term adherence and positive psychosocial outcomes.

Limitations

Limitations of this research should be acknowledged. This trial was powered to assess feasibility of a complex survivorship intervention rather than the treatment effect of dietetic input, so caution is warranted when interpreting outcomes related to body composition and dietary quality. In addition, individual clinical intentions regarding weight management (e.g. weight loss, weight maintenance, or prevention of weight

gain) were not captured as part of the study protocol. As a result, it was not possible to explore whether body composition changes differed according to participant intent, which may have contributed to heterogeneity in observed outcomes. Future adequately powered trials should consider incorporating predefined classification of participant weight management goals to enable more nuanced interpretation of intervention effects. Limited resources occasionally led to cancellation of trigger-initiated consultations due to clinical capacity constraints, which may have negatively influenced outcomes. Despite these limitations, they provide important insights for future study design.

Implications and Future Directions

These findings underscore the need for multidimensional, survivorship-specific screening tools to capture treatment- and symptom-related nutritional risks and guide targeted dietetic interventions. Future work should address low-responding dietary components and key risks such as weight gain, iatrogenic menopause, and cardiovascular complications, integrating dietetic consultations with nurse-led assessments and multidisciplinary supports to enhance adherence. Refining symptom- and BMI-trigger pathways, embedding behaviour change strategies, and documenting dietitian time will inform resource allocation, cost-effectiveness, and scalable service delivery. Leveraging ePROs can personalise care, streamline workflows, and facilitate patient-centred interventions. Collectively, these strategies provide a foundation for proactive, tailored survivorship services and fully powered, co-designed clinical trials.

4.7 CONCLUSION

This randomised controlled trial demonstrates that a trigger-based, ePRO-initiated dietetic intervention is feasible, well-accepted, and capable of reducing patient-

reported weight gain concern among early-stage breast and gynaecologic cancer survivors, even in the absence of significant changes in body composition or dietary quality. Good engagement and attendance highlight the potential of personalised, symptom-responsive counselling to positively influence perceptions of weight management and reduce weight-related stigma. The findings also underscore limitations of existing screening tools, the complexity of managing dual interventions, and the substantial resource requirements involved. Importantly, these results provide a foundation for developing standardised, resource-efficient, survivorship-specific dietetic services, with tailored trigger pathways and multidimensional screening approaches. A fully powered randomised controlled trial, informed by these feasibility insights, is warranted to optimise delivery, evaluate long-term dietary and psychosocial outcomes, and support evidence-based guidelines for dietetic care in cancer survivorship.

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CHAPTER 5: A YEAR LONG LENS: LONGITUDINAL PATTERNS IN DIETARY AND HERBAL SUPPLEMENT USE AMONG EARLY-STAGE BREAST AND GYNAECOLOGIC CANCER SURVIVORS – *RESULTS FROM THE LINKING YOU TO SUPPORT AND ADVICE "LYSA" RANDOMISED CONTROLLED TRIAL*

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5.1 ABSTRACT

Background: Supplement use is common among cancer survivors for wellbeing, symptom management, or coping, despite guidelines advising against routine use without deficiency. This study examined changes in vitamin-mineral and herbal-botanical supplement use over 12 months in early-stage breast and gynaecologic cancer survivors, and identified associated demographic, clinical, and symptom factors.

Methods: In this secondary analysis of an unblinded randomised feasibility trial at two Irish cancer centres, 200 women ≤12 months post-curative treatment were assigned to usual care or a survivorship clinic. Supplement use was assessed at baseline and 12 months via the EPIC-Norfolk Food Frequency Questionnaire. Analyses were conducted in R, using descriptive and inferential statistics stratified by cancer type, education, endocrine therapy, BMI, and symptoms ($p < 0.05$).

Results: Of 200 participants, 187 completed baseline and 162 the 12-month follow-up. Overall supplement use remained high, increasing from 84% to 87% ($p < 0.01$). Vitamin D, calcium, and multivitamins were most common; herbal-botanical use rose from 21.9% to 26.5%, led by Evening Primrose Oil. Higher use was associated with breast cancer diagnosis ($p < 0.05$), education level ($p < 0.05$), physical activity ($p < 0.01$), fatigue ($p < 0.01$), and hot flash severity ($p < 0.05$), while severe joint pain and reduced libido were associated with lower use. Diversity and frequency of supplements increased, notably fish oil, magnesium, and turmeric.

Conclusions: Supplement use is prevalent and grows over time, reflecting active self-management and varying by cancer type, education, and symptoms.

5.2 INTRODUCTION

Dietary (vitamin and mineral) and herbal botanical supplement use is prevalent in cancer survivors, with up to 85% reporting their use (1). In the last two decades, there has been a large increase in dietary supplement use in individuals diagnosed with cancer (2), despite international bodies discouraging their use in this population. The European Society of Clinical Nutrition and Metabolism (ESPEN) Clinical Cancer Guideline discourages the use of high dose micronutrients in the absence of specific deficiency (3), whilst the World Cancer Research Fund's Recommendations for Cancer Prevention, and Survivorship, does not support the use of supplements for cancer prevention or as a means of improving survival (4). Yet, cancer survivors are still engaging in supplementation.

Food and dietary supplements, as defined by the European Food Safety Authority and the U.S. Food and Drug Administration, are concentrated sources of nutrients or other substances with nutritional or physiological effects, typically consumed in measured forms such as pills, capsules, or liquids (5,6). While regulations differ - EU classifies them as foodstuffs and the US as dietary products unless used to treat disease - they commonly include vitamins, minerals, amino acids, botanicals, and other compounds (7,8). Common reasons cited for dietary and herbal supplement use in oncology populations include improving or maintaining overall health and wellbeing (9–15); prevent health problems or disease (9,14,15); manage adverse effects of anti-cancer therapies (10–12,16–18); improve appearance or performance (11,12); something survivors can do for themselves (19); boost immune system (13–15,17,19); improve quality of life or act as coping mechanism (13,17); or improve the efficacy of systemic anti-cancer treatments (16).

Sarradon-Eck et al., (12) observed that cancer patients and survivors use non-conventional medicines, including dietary and herbal supplements, as a complementary coping strategy, which may indicate a potentially impaired quality of life to healthcare professionals (12). Historically, cancer survivors do not typically disclose supplement use to their healthcare providers (1). In five international studies, between 21.6% and 46.1% did not consult or disclose their supplement use to their healthcare provider, citing that the physician did not ask or they felt that the physician did not need to know (9,11,16,18,20).

Multiple large cohorts, including the National Health and Nutrition Examination Survey (NHANES) data (1999-2016), shows that dietary supplement use among cancer survivors is common, with prevalence ranging from around 30% to over 70% depending on the population and region (2,11,17,21–23). Use is consistently associated with female gender, older age (2,17), higher education (2,19), better self-reported health (2,19), and specific cancer types such as breast (2,9–11) and gynaecologic cancer (10,17,24). Breast cancer survivors notably report high supplement use, often involving multiple products, including vitamin, mineral and herbal supplements (23,24,27–29). However, many use supplements without consulting healthcare providers and some have lower nutrient intake from foods, despite supplementation (9). International studies reflect similar patterns, with some evidence associating supplement use to ongoing cancer treatment (26,28,30), fear of recurrence (31) and long-term side effects (17). Importantly, there are concerns about contraindicated supplement use (11) and rising prevalence of non-conventional medicine use post-diagnosis (12,16,31,32).

Literature surrounding changes to dietary supplement use after cancer in Ireland is limited. In 2013, Fox et al (33) surveyed 406 breast cancer survivors, highlighting

55.7% used complementary and alternative medicines; 18.5% used herbal medications, 14.5% used health supplements and 2.7% used high dose vitamins (33). In a 2021 survey of 1073 Irish cancer survivors (n = 362 breast), 36.9% reported using complementary and alternative medicines, with 23.6% using dietary supplements and 6.3% using herbal remedies. More recently, a 2024 cross sectional survey (n = 185) showed that 45% of breast cancer survivors were regular supplement users (34). In line with international literature, regular supplement use post cancer diagnosis was associated with a higher education level ($p = 0.05$) (34).

A major concern regarding supplement use during ongoing adjuvant endocrine therapy is the potential for drug-nutrient or drug-herb interactions. While literature on supplementation in breast cancer is emerging few studies have examined these interactions in depth. Harrigan et al. (2021) highlighted, for the first time, dietary supplement use and its potential interactions with adjuvant endocrine therapies in breast cancer survivors (29). Notably, the study reported that, of 108 self-reported dietary products, one-third of the individual ingredients had potential interactions with endocrine therapies (29). More recently, in 2024, the Heads of the European Food Safety Agencies published a report evaluating 117 individual supplements, identifying thirteen that posed harmful risks to human health - including several commonly used by breast cancer survivors (35).

Few studies have examined changes in supplement use over time in cancer survivors, with most relying on cross-sectional data collected at a single time point. Tracking supplement use over 12 months in the early survivorship phase allows this study to capture patterns related to symptoms, treatment side effects, and other factors that one-time surveys cannot detect. Understanding these longitudinal patterns is particularly

important for individuals on long-term endocrine therapy who may continue managing side effects for years after primary treatment.

5.3 AIMS AND OBJECTIVES

Building on this gap in knowledge, the current secondary analysis of the Linking You to Support and Advice (LYSA) Trial aims to characterise the longitudinal use of vitamin-mineral and herbal-botanical supplements over a 12-month period, including type, frequency, and dosage, in a cohort of early-stage hormone receptor-positive breast and gynaecologic cancer survivors. A secondary aim is to explore differences in supplement use patterns across demographic and clinical variables.

5.4 METHODS

5.4.1 Trial Design and Setting

The *Linking You to Support and Advice* (LYSA) Trial was an unblinded, parallel arm study with a randomised controlled design (experimental and active comparator arm) in two regional cancer centres in the Republic of Ireland (36). It assessed the feasibility of a nurse- and dietitian-led survivorship clinic utilising electronic patient reported outcomes in early-stage breast and gynaecologic cancer patients. It met its pre-defined feasibility outcomes.

The primary LYSA Trial protocol (36), along with the accompanying dietetic protocol (37) have been published previously.

5.4.2 Participants

Participants enrolled (n = 200) had a diagnosis of early-stage hormone receptor positive breast or gynaecologic cancer who were less than 12 months post-primary curative treatment.

5.4.3 Research Ethics

The trial received full ethical approval from both sites from the appropriate clinical research ethics committee and was conducted in adherence with the Declaration of Helsinki and ICH6 Good Clinical Practice.

5.4.4 Intervention

All participants underwent cancer-specific quality of life and nutritional assessments at their baseline (T0) and endpoint (T12) clinic. These included items from the European Organisation for Research and Treatment of Cancer Quality of Life (EORTC QLQ-C30) tool (38) and Patient Report Outcome Common Terminology Criteria for Adverse Events (PRO-CTCAE) tool (39), assessment of fear of recurrence, body mass index (BMI), weight gain concern, self-reported physical activity levels using the Nordic Physical Activity Questionnaire (NPAQ)-short questionnaire (40) and a Food Frequency Questionnaire (FFQ) (41,42).

Data were collected at baseline on a range of demographic, clinical, and lifestyle variables. Age was categorised into three groups: <40 years, 40-54 years, and ≥55 years. Time from diagnosis to study entry was grouped as <6 months, 6-12 months, and >1 year up to 2 years. Menopausal status was recorded as premenopausal, perimenopausal, postmenopausal, or unknown. Menopausal status was determined by patient reported menstrual history or as documented in medical notes from their first medical oncology visit. Clinical data included primary tumour location, history of surgery, chemotherapy, radiotherapy, and endocrine therapy regimen. Body mass index (BMI) was classified as underweight (<18.5kg/m^2), normal weight (18.5-24.9kg/m^2), overweight (25.0-29.9kg/m^2), or obese (≥30kg/m^2) (43). Additional sociodemographic variables included marital status, ethnicity, education level

(primary, secondary, or third level), baseline economic status and perceived economic certainty.

5.4.5 Assessment of Supplement Use

Dietary supplement use was assessed at baseline (T0) and 12 month follow up (T12) using an FFQ, a validated tool designed to capture habitual intake of foods and supplements over the preceding 12 months (42). Participants were asked to report the frequency of use for vitamins, minerals and other dietary supplements. The FFQ was administered in paper format and reviewed for completeness by research dietitians.

Responses to the question "Have you ever taken any vitamin, mineral, fish oils, fibre or other food supplements during the past year. Responses were categorised as "*Yes*" (regular use); "*No*" (no use); "*Sometimes*" (occasional use) and "*Don't Know*" and then numerically coded for analysis (Supplementary Table 5.1).

Participants who answered "*Yes*" or "*Sometimes*" were invited to complete a table detailing up to eight of their most frequently used supplements, including brand, supplement name, strength per unit, number of units consumed per day, and average frequency over the past year. Frequency responses were categorised and coded for analysis (Supplementary Table 5.1).

5.4.6 Data Management

Throughout the study, completed FFQs were maintained in the Trial Master File and, upon study completion, filed into participants' medical records in accordance with hospital policy. The FFQ EPIC Tool for Analysis (FETA) template, with all extracted supplement data, was uploaded to the electronic Trial Master File, duplicated onto secure removable media, and archived in line with sponsor guidelines.

5.4.7 Supplement Data Extraction and Processing

Data on dietary supplement use were extracted from the FFQ using FETA output (44). The supplement-related variables were isolated from the full dietary dataset, and entries were manually reviewed for consistency and completeness by the research dietitian. Cleaning involved correcting data entry errors, resolving ambiguous responses and excluding incomplete entries. Supplement use was then categorised by type (multivitamin, single nutrient supplements, herbal botanical supplements and vitamin mineral-herbal botanical blends), frequency of use and dosage. These categories were coded into a new structured dataset for analysis using the same numerical coding as the FETA template for frequency of use. Coded variables included binary indicators (use vs no use), frequency categories and total number of supplements used.

5.4.8 Statistical Analysis

Data were cleaned and analysed using R (version 4.5.0) (45) primarily with the "*tidyverse*" suite of packages, including *dplyr* and *tidyr*. Descriptive statistics summarized participant characteristics and supplement use patterns. Continuous variables were summarised using means with standard deviations (SD) or medians with interquartile range as appropriate based on data distribution. Categorical variables were presented as frequencies and proportions.

Supplement use (vitamin/mineral and herbal/botanical) was reported overall and stratified by key variables including cancer type (breast, cervical, endometrial), study arm (active comparator versus experimental), endocrine therapy status, age, treatment history, education level, and BMI. Cross-tabulations examined the co-occurrence of supplement use among participants.

Associations between demographic, clinical factors and supplement use at baseline (T0) and follow-up (T12) were assessed using; Wilcoxon, Kruskal-Wallis, Pearson's Chi-Squared, McNemar's Chi-Squared and Fisher's Exact tests, as appropriate. Post-hoc analyses of significant P values were conducted using Dunn's test with Bonferroni adjustments and Chi-square tests for residual analysis. Results were interpreted based on test assumptions, with significance defined as a two-sided p-value of < 0.05 or < 0.01.

5.5 RESULTS

5.5.1 Participant Characteristics

Of 200 participants enrolled, a full data set was available for 187 participants at baseline (T0), and 162 participants at endpoint (T12), n = 13 had dropped out of the study and n = 12 did not complete the FFQ. Of 187 participants, 157 (85.5%) had a breast cancer diagnosis, 12 (6.4%) had a cervical diagnosis and 17 (9.1%) had an endometrial diagnosis (Table 5.1). The median age of participants was 54 years (range: 23-78 years). At baseline, 56.7% of participants were between 6 months and 1 year since their diagnosis, 31.2% were premenopausal and 43% were prescribed anastrozole as their endocrine therapy (Table 5.1). The mean body mass index (BMI) was 28.5 (SD ± 6.69).

Table 5.1. Baseline Clinicopathologic and Sociodemographic Characteristics

Characteristic	**N = 187**
Age	**% (n)**
< 40 years	6.4 *(12)*
40 – 54 years	43.9 *(82)*
≥ 55 years	48.1 *(90)*
Time from Diagnosis to T0 (0 Months)	**% (n)**
Less than 6 months	23.5 *(44)*
Between 6 months and 1 year	56.7 *(106)*
More than 1 year up to 2 years	19.8 *(37)*
Primary Tumour Location	**% (n)**
Breast	84.5 *(158)*
Cervical	6.4 *(12)*
Endometrial	9.1 *(17)*
Treatment History	**% (n)**
Chemotherapy	60.4 *(113)*
Endocrine Therapy	84.0 *(157)*
Radiotherapy	98.9 *(185)*
Surgery	95.2 *(178)*
Endocrine Therapy Regimen	**% (n) ***
Anastrozole	43.7 *(67)*
Anastrozole/Goserelin	5.1 *(8)*
Exemestane	4.5 *(7)*
Exemestane/Goserelin	1.9 *(3)*
Letrozole	7.0 *(11)*
Tamoxifen	36.9 *(58)*
Tamoxifen/Goserelin	1.9 *(3)*
Menopausal Status	**% (n)**
Pre	32.1 *(60)*
Peri	10.7 *(20)*
Post	55.1 *(103)*
Unknown	2.1 *(4)*

Body Mass Index	**% (n)**
Underweight (<18.5kg/m^2)	1.1 *(2)*
Normal (18.5-24.9kg/m^2)	31.6 *(59)*
Overweight (25.0-29.9kg/m^2)	32.6 *(61)*
Obese (≥30.0kg/m^2)	34.8 *(65)*
Ethnicity	**% (n)**
White Irish	92.0 *(172)*
Any other white background	7.0 *(13)*
Any other Asian background	0.5 *(1)*
Chinese	0.5 *(1)*
Education Level	**% (n)**
Primary level	2.7 *(5)*
Secondary level	32.6 *(61)*
Third level (college/university)	64.7 *(121)*
Employment Status	**% (n)**
Employed	29.9 *(56)*
Unable to work due to sickness or disability	28.9 *(64)*
Unemployed, looking for a job	2.1 *(4)*
Retired	17.6 *(33)*
Unable to work due to COVID restrictions	5.3 (*1)*
Other reasons	2.1 *(4)*
Unemployed, looking for a job	2.1 *(4)*
Student	1.6 *(3)*
Unemployed, not looking for a job	1.6 *(3)*
Economic Certainty	**% (n)**
Coping on present income	42.2 *(79)*
Living comfortably on present income	38.0 *(71)*
Difficult on present income	12.8 *(24)*
Very difficult on present income	5.8 *(11)*
Rather not say	1.1 *(2)*
Marital Status	**% (n)**
Married	62.0 *(116)*
Single	15.0 *(28)*

Cohabiting	7.5 *(14)*
Separated	5.3 *(10)*
Widowed	5.3 *(10)*
Divorced	4.8 *(9)*

*n/157

Abbreviations: kg/m^2: kilogram per metres squared

5.5.2 Supplement Use at Baseline

At baseline, 84% (n = 157) reported using any vitamin or mineral supplement. Approximately one fifth of participants (21.9%) reported the use of an herbal botanical supplement. The mean number of supplements used was 2.39 (±1.90), with 52.9% (n = 111) using 1 – 3 supplements and 24.6% (n =4 6) using 4 – 8 supplements. Breast cancer survivors reported the highest supplement use (84%, n = 133), followed by endometrial (71%, n = 12) and cervical cancer survivors (58%, n = 7). The most frequently used vitamin/mineral supplement was Vitamin D (41.18%), followed by Calcium and Vitamin D Combination (36.9%), and Multivitamin (33.16%) (Table 5.2). Most herbal botanical users combined them with vitamin and mineral supplements, with no participants reporting the use of herbal botanicals alone (Table 5.3). The most used herbal botanical supplement was Evening Primrose Oil (10.2%), followed by Turmeric/Curcumin (4.3%) (Table 5.4). Daily use was reported for several supplements, including the Calcium and Vitamin D combination (14%), Vitamin D (16%), multivitamins (12%), and Evening Primrose Oil (6%) (Supplementary Table 5.2).

Sixteen different herbal and botanical supplements were used by participants at baseline. At baseline, vitamin and mineral supplement use was significantly associated with primary tumour location ($p < 0.05$) and fatigue levels ($p < 0.05$) (Figure 5.1). No statistically significant associations were observed between herbal botanical

supplement use and any demographic or clinical variables, including time since diagnosis, education, primary tumour location, economic status and menopausal status.

Daily users of all types of supplements at baseline (n = 86) tended to be between the age of 45-54 years (26%); postmenopausal (65%); have a BMI between 18.5kg/m^2 to 24.9kg/m^2 (35%) and 64% of daily supplement users reported weight gain concern. Daily users also reported an EORTC score of 50 – 59 (36%). They also tended to have lower physical activity levels, with 41% undertaking less than 75 minutes of moderate-to-vigorous activity per week.

Table 5.2: Most Frequently Used Vitamin Mineral Supplements Used Over 12 Months

Vitamin or Mineral Supplement	**Month 0 Use n [n = 187] (%)**		**Month 12 Use n [n = 162] (%)**		**P value**
Any Vitamin or Mineral Supplement	157	*(83.96)*	137	*(84.57)*	**<0.01**
Vitamin D	77	*(41.18)*	52	*(27.81)*	**<0.01**
Calcium & Vitamin D Combination	69	*(36.90)*	47	*(25.13)*	**<0.01**
Multivitamin	62	*(33.16)*	39	*(20.86)*	**<0.01**
Vitamin C	27	*(14.44)*	20	*(10.70)*	0.28
Fish Oils	23	*(12.30)*	24	*(12.83)*	1
Probiotic	20	*(10.70)*	10	*(5.35)*	**<0.05**
Magnesium	16	*(8.56)*	27	*(14.44)*	**0.05**
Calcium	12	*(6.42)*	20	*(10.70)*	0.15
Vitamin B Complex	12	*(6.42)*	11	*(5.88)*	1
Iron	8	*(4.28)*	4	*(2.14)*	0.29

Participants reporting a severe decreased libido used significantly fewer supplements than those with mild or no decreased libido ($p < 0.05$). Of note, participants who used herbal botanical supplements at baseline were significantly more likely to report moderate general pain and less likely to report no pain ($p < 0.01$), in addition to being

more likely to report severe abdominal pain and less likely to report no abdominal pain ($p < 0.05$). Physical activity also influenced supplement use; participants engaging in less than 75 minutes per week of moderate-to-vigorous activity used fewer supplements, whereas herbal botanical supplement users were more likely to engage in over 150 minutes per week ($p < 0.05$).

5.5.3 Supplement Use at Endpoint

At 12 months, supplement use remained high, with 141 of 162 participants (87%) reporting use. The mean number of supplements used was 2.25 (±1.86). A statistically significant increase in the number of supplements used was observed between baseline and endpoint ($p < 0.01$). At endpoint, 66% (n = 107) participants used between 1 – 3 supplements, whilst only 21% (n = 34) used between 4 – 8 supplements. Participants with a breast cancer diagnosis used the greatest number of supplements (mean: 2.34 ±1.93); followed by those with endometrial cancer (mean: 1.92 ±1.44) and cervical cancer (mean: 1.55 ±1.13). Daily use increased for several supplements, including the Calcium and Vitamin D combination (26%), Calcium alone (9%), Evening Primrose Oil (11%), Fish Oils (11%), Magnesium (12%), multivitamins (15%), multivitamin-herbal blends (5%), Vitamin B3 (4%), and Vitamin C (7%). Herbal botanical supplement use increased to 26.5%, with Evening Primrose Oil remaining the most commonly used.

Table 5.3: Use of Vitamin Mineral in Combination with Herbal Botanical Supplements over 12 Months

Use of Vitamin Mineral Supplement	Use of Herbal Botanical Supplements	Month 0 n [n = 187] (%)	Month 12 n [n = 162] (%)
No	No	30 *(16)*	21 *(13)*
Yes	No	116 *(62)*	98 *(61)*
Yes	Yes	41 *(21)*	39 *(24)*
No	Yes	0 *(0)*	4 *(2)*

The percentage of participants using a combination of Vitamin Mineral and herbal botanical supplementation increased from baseline (22%) to endpoint (24.1%) (Table 5.3). Vitamin and Mineral supplement use at endpoint was significantly associated with education level ($p < 0.05$), with higher use among participants with third level education. Daily supplement users at endpoint (n = 112) had a similar profile as baseline. Daily users tended to be aged between 45-54 years (29%); postmenopausal (59%); have a BMI between 18.5kg/m^2 to 24.9kg/m^2 (27%) and 25.0kg/m^2 to 29.9kg/m^2 (22%); third level educated (69%); reported mild to moderate symptoms; and were less active (Supplementary Table 5.3). In a change from baseline, endpoint daily supplement users were more likely to be coping on present income (44%) and had a lower self-reported EORTC score of 40-49 (38%).

Table 5.4: Most Frequently Used Herbal Botanical Supplement Use Over 12 Months

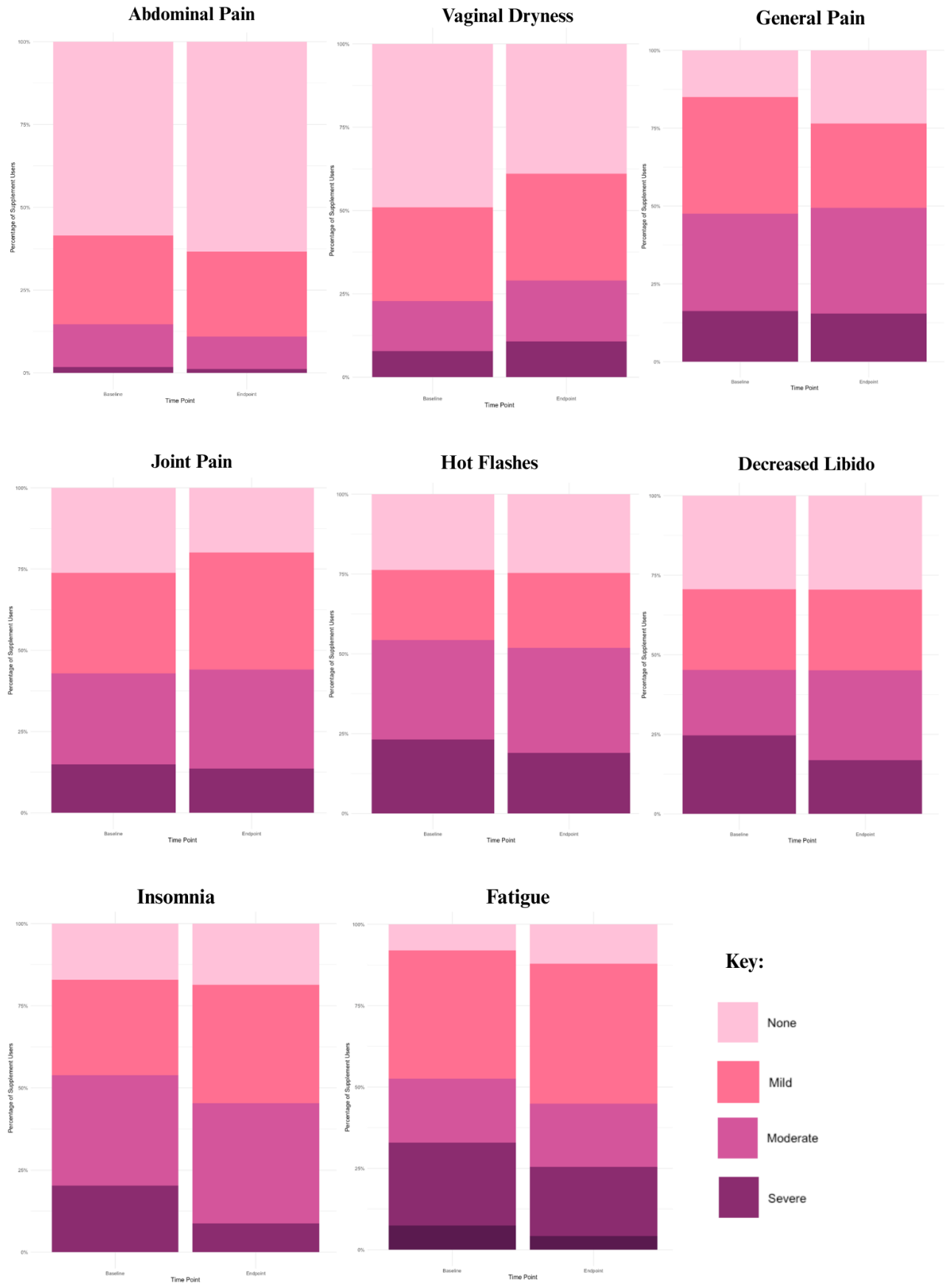
Herbal And Botanical Supplement	Month 0 N [n = 187] (%)		Month 12 N [n = 162] (%)		Change (PP)
Any Herbal Botanical Supplement	41	*(21.93)*	43	*(26.54)*	+4.6
Evening Primrose Oil	19	*(10.16)*	19	*(11.73)*	+1.5
Turmeric or Curcumin	8	*(4.28)*	5	*(3.09)*	-1.2
Multivitamin and Herbal Botanical Blend	6	*(3.21)*	11	*(6.79)*	+3.6
Other Botanicals* (<3% each)					

Abbreviations: PP; percentage point *Other botanicals = Red Yeast Rice, Sage

At endpoint, there was a significant association between patient reported hot flash severity and the number of supplements use ($p < 0.05$), those with severe hot flashes used more supplements than those with mild hot flashes. Furthermore, participants who reported severe hot flashes used more Vitamin and Mineral supplements compared to those who reported mild hot flashes ($p < 0.01$). Contrastingly, participants who reported severe joint pain used significantly fewer supplements compared to those who reported no joint pain ($p < 0.01$). Participants using herbal and botanical supplements were more likely to report 75 – 150 minutes a week of moderate to vigorous activity and less likely to report <75 minutes of moderate to vigorous activity ($p < 0.05$).

5.5.4 Dosages of Supplements Used

Calcium and Vitamin D supplement dosages varied among participants, with most taking 1000mg Calcium/800IU Vitamin D at both baseline (59.4%) and endpoint (64%), while Vitamin D dosages ranged widely from 200IU to 75,000IU at baseline and 1000IU to 50,000IU at endpoint. Evening Primrose Oil and Turmeric/Curcumin supplement dosages decreased over time, with 1000mg being the most common dose for Evening Primrose Oil users. Notably, all Sage supplement users consistently reported a 51mg dosage at endpoint.



Footnote: Y Axis "Percentage of Supplement Users"; X Axis "Timepoint, Baseline and Endpoint".

Figure 5.1. Patient Reported Severity of Symptoms in Supplement Users at Baseline and Endpoint

5.6 DISCUSSION

The findings indicate supplement use was highly prevalent in the LYSA cohort, with 84% of participants reporting use at baseline, increasing 12 months later to 87%. Breast cancer survivors reported the highest supplement use compared to those with cervical or endometrial cancer, with a significant association between primary tumour location and vitamin/mineral supplement use at baseline ($p = 0.05$). This aligns with the literature, Abdel-Rahman (2021) and Du et al. (2020), reported from NHANES data that people affected by breast and uterine cancers had an increased average use of any-type of supplement (2,9). Similarly, Kaur et al. (2022) (10) and Kristoffersen et al. (2024) (17) reported that supplement use was significantly associated with female genital cancers. Interestingly, Hauer et al. (2023) (28) and Saquib et al. (2011) (26) highlighted that those with a hormone receptor positive subtype and recipients of endocrine therapy were more likely to use dietary supplements. In the European context, the NutriNet-Santé cohort (n = 1,081) reported 62% of female cancer survivors using dietary supplements, with 68.3% of those diagnosed with breast cancer reporting supplement use (11). In the Irish context, data around longitudinal use is limited; findings from 2024 (n = 185) suggested that regular supplement use amongst breast cancer survivors was 45% (34), lower than that of the LYSA cohort. To our knowledge, this is one of the first Irish longitudinal studies to characterise supplement use across multiple cancer survivor groups within a structured survivorship intervention, providing contemporary prevalence estimates in this population.

Over the 12-month period of the LYSA trial, there was an increase in both the number and variety of supplements used, particularly herbal and botanical products, with uptake of sixteen different types. The proportion of participants reporting no supplement use declined from 19.1% to 14.9%, while those using 1-3 supplements

rose from 52.9% to 66%. Use of 4-8 supplements remained relatively stable at approximately 21%. These patterns are consistent with findings from American studies of cancer survivors. Harrigan et al. (2021) found that 51% of breast cancer survivors used ≥3 individual supplements, and 23% used ≥5 (10). In a 2023 study (n = 1271), Hauer et al. (2023) highlighted high prevalence closer to that of the LYSA cohort, highlighted 89.5% of breast cancer survivors reported vitamin and mineral use and 67.7% reported natural product use herbal botanical supplement use (28). Findings reported that 46.5% of vitamin and mineral users and 26.7% of herbal botanical supplement users reported at least three products concurrently (28). This literature points to the increasing prevalence of supplement use in breast cancer survivors over the past decade. The mean number of dietary supplements used in the French NutriNet-Santé cohort (2015) was less than that reported in the US, at 1.9 (±1.4), and less than that reported by the LYSA cohort at baseline and endpoint (2.39 ±1.90; 2.25 ±1.86), alluding to the increasing use of supplements over the past decade (11,28,29). Looking back to the Irish context over the last decade, a 2013 survey (n = 406), 55.7% reported complementary and alternative medicine use, with 18.5% using herbal medicines, 14.5% using health supplements and 2.7% using high dose vitamins (33), again a large decrease from the LYSA cohort findings. The differences in these findings may be attributed to a number of factors: underreporting to healthcare professionals or researchers; an upward trend in supplement use over the past decade; differences in acceptability and access to supplement use globally. Nevertheless, the upward trend in supplement use represents a call to action for clinicians of all disciplines: to prioritise inquiry about supplement practices, strengthen their knowledge base, and provide balanced, unbiased education to service users navigating survivorship care. These longitudinal findings add novel evidence demonstrating

changes in both the number and diversity of supplements used over time within a cancer survivorship cohort, an area that remains under-reported in existing literature.

The most commonly used supplements were vitamin D, calcium with vitamin D, and multivitamins, with a significant increase in the number of supplements used over time. The highly prevalent use of calcium and vitamin D supplements may reflect adherence to oncology clinical guidelines (46,47) which recommend supplementation for those on endocrine therapy (46), a group that included 84% of this cohort. This data is promising, highlighting good adherence and attention to bone health, given the 7.7% higher risk of elevated risk of treatment related bone loss in postmenopausal breast cancer survivors, compared with the general population (48). These findings are consistent with recent Irish data from 2024, showing increased calcium and vitamin D use after diagnosis (34), and with international literature (10,22).

Another important consideration for clinicians is the risk of excessive intake, particularly of fat-soluble vitamins such as vitamin D, which can accumulate in the body over time. This issue is directly relevant to the LYSA cohort, where the three most commonly reported supplements were vitamin D, calcium-vitamin D combinations, and multivitamins. Excessive intake, especially when obtained from multiple preparations such as single supplements, combination products (e.g., calcium with vitamin D), or multivitamins, raises legitimate concerns regarding potential toxicity. The highly prevalent use of multivitamins may reflect the want to support or maintain general wellbeing and overall health (10–13), though future research is needed to understand the motivators for individual supplement use in breast and gynaecologic cancer survivors.

Herbal and botanical supplement use also increased over 12 months, though to a lesser extent than vitamin mineral use, with evening primrose oil remaining the most frequently used product (with ~10% of the LYSA cohort reporting its use at baseline and endpoint) typically for hot flashes. Evidence for the efficacy of evening primrose oil remains insufficient, as highlighted in a recent 2024 systematic review and meta-analysis (49). Despite this, usage continues to rise following diagnosis of breast cancer, including in the UK DietCompLyf study (23). Although not a primary outcome of this analysis drug-herb interactions are a key concern in this cohort. Harrigan et al. (2021) reported on dietary supplement use and interactions with tamoxifen and aromatase inhibitors in breast cancer survivors enrolled in lifestyle trials, highlighting that 38% were taking a dietary supplement with a potential risk of interactions (29). Applying this to the LYSA cohort, 40.7% of herbal supplements reported - cranberry extract, echinacea, garlic extract, ginseng, maca root, milk thistle, quercetin, red yeast rice, rhodiola root, slippery elm bark and turmeric - have potential interactions with endocrine therapies. Furthermore, the use of fourteen herbal botanical supplements increased over 12 months and three of these (ashwagandha, maca and turmeric) have been flagged as potentially harmful by a 2024 European Food Safety Agency Report (35). These findings should be of concern to healthcare professionals, and further highlight the need for regular supplement assessment to mitigate potential drug/herb risks.

While clinical factors such as symptom burden and guideline adherence strongly influence supplement use, demographic and lifestyle variables, such as education and physical activity, may further explain variation in uptake, warranting closer examination. Education level was significantly associated with vitamin and mineral supplement use at 12 months ($p < 0.05$), with higher usage observed among

participants with third-level education. Literature globally has associated higher education levels with dietary supplement use in this cohort. In NHANES data, supplement use was significantly associated with higher education levels (*OR: 0.59; 95% CI: 0.56-0.63*) (1). Furthermore, Ferruci et al., 2009 study reported that higher education level was significantly associated with supplement use (19). Likewise, in a cohort of Korean breast cancer survivors higher education level was significantly associated with supplement use ($p = 0.02$) (21).

Interestingly, using data from the *HEAL* study, Ma et al. (2011) reported that participants who used oestrogenic botanical supplements were more likely to have a higher education status (27). Aligning with recent Irish data, O'Donovan et al. (2024) highlighted that higher education level was significantly associated with post-diagnosis supplement use ($p = 0.05$) (34), further supporting prior research indicating that more educated individuals are more likely to engage in proactive health management (2,19,21,26,34). These findings may be attributed to participants in clinical trials tending to have a higher education level. However, clinicians should not assume that patients with higher education automatically make informed choices. All patients, regardless of education level, benefit from clear guidance and discussion about supplement use. Physical activity also emerged as a strong predictor in the LYSA cohort, particularly in relation to herbal supplement use. Higher levels of physical activity were consistently associated with greater use of both vitamin/mineral and herbal botanical products ($p < 0.05$). Survivors achieving ≥75 minutes of moderate-to-vigorous activity per week were significantly more likely to use supplements at both time points. This association may reflect an overall orientation toward health-promoting behaviours among more active individuals, consistent with prior findings linking supplement use to other positive lifestyle practice (2,11,12,19).

Literature has previously suggested that cancer survivors turn to supplements to offer symptom relief (10–12,16–18) and improve quality of life (13,17). Marian (2017) noted that consumers are drawn to supplements, particularly botanicals, as they are natural, and therefore considered safe to assist in symptom management and improving quality of life (1). In the LYSA cohort, supplement use appeared to reflect distinct symptom burden profiles, suggesting that survivors may be using supplements as a strategy to manage persistent and bothersome symptoms. This is particularly relevant for clinicians, as participants with a hormone receptor positive subtype of breast cancer are contraindicated for the use of hormone replacement therapy, usually prescribed to reduce symptom burden in menopause (46,50). Donohoe et al. (2023) reported that up to 50% of women use non-pharmacologic therapies to manage menopausal symptoms, many of which are not supported by high quality evidence (51). The severity of menopausal symptoms is a common reason for endocrine therapy discontinuation: in a cohort of New Zealand breast cancer survivors (n = 1,213) adherence to endocrine therapy dropped from 90% during the first year of therapy to 50% at the fifth year, with 20% citing adverse events or poor tolerability as reasons for discontinuation (52). Interestingly, in the LYSA cohort, daily supplement users of any type more often reported mild or moderate symptoms and lower self-reported quality of life (Figure 5.1) suggesting that survivors may adopt supplements as an early, self-directed strategy to manage symptoms and prevent progression to severe discomfort.

Greater fatigue severity was linked to higher overall supplement use ($p < 0.05$) and survivors with severe hot flashes reported markedly greater use of vitamin and mineral supplements ($p < 0.01$). These patterns reinforce prior evidence that cancer survivors frequently turn to supplements to address fatigue, vasomotor symptoms, and pain

when pharmacologic options are limited or ineffective (53,54). Interestingly, a systematic literature review of 113 randomised controlled trials reported that use of dietary supplement did not improve cancer-related fatigue during or after treatment (55). This suggests a possible placebo effect, given the association of use in this cohort, warranting further investigation for reasons for supplement use in alleviating symptom burden and perceived effectiveness. There is increasing data around the use of evening primrose oil and soy isoflavones in the treatment of hot flashes and vasomotor symptoms. A 2016 systematic review and meta-analysis reported an improvement in the number of daily hot flashes with specific phytoestrogen supplementation (pooled mean difference of changes, *-0.79 [95% CIs: -1.35 to -0.23]*) (56). Whilst these seems promising there is a significant clinical consideration in the use of high-dose phytoestrogen supplementation in hormone-receptor positive cancers, due to a lack of safety data in this population relating to recurrence risk in this subtype. Furthermore, there is limited data reporting the prevalence of supplement use and the severity of vasomotor symptoms in oncology cohorts, highlighting the need for future research to focus on safety, motivators, patient reported perceived effectiveness and sources of information.

In contrast, severe joint pain and decreased libido were linked to lower supplement use ($p < 0.01$ and $p < 0.05$). Survivors reporting severe libido loss were also less likely to use supplements, a novel finding warranting further investigation into potential psychological or relational influences on health behaviour engagement. Herbal and botanical supplement use was more common among those experiencing moderate general pain ($p < 0.01$) and severe abdominal pain ($p < 0.05$). Herbal supplement use was more prevalent among survivors reporting moderate general pain and severe abdominal pain at baseline, whereas those with severe joint pain at 12 months reported

fewer total supplements. Again, data reflecting the prevalence of herbal supplement use and severity of symptoms is limited. However, these opposing trends may suggest symptom-specific motivations, which has been well reported in the literature (10–13,16–19). A key novel finding of this study is the observed association between symptom burden profiles and specific patterns of supplement use, suggesting that supplement behaviours may be closely linked to symptom self-management strategies within survivorship care.

In our study, primary tumour location influenced supplement use, with breast cancer survivors more likely to report use at both time points, potentially reflecting differing symptom experiences, and aligning with current international literature (2,9,10,28). In contrast, herbal supplement use in our study showed no significant associations with demographic or clinical variables; however, this may reflect insufficient statistical power rather than a genuine absence of underlying patterns, as the LYSA Trial was powered to assess feasibility rather than supplement use. These findings underscore the complex interplay of demographic, clinical, and symptom-related factors in shaping supplement use patterns among cancer survivors, highlighting the importance of comprehensive and individualised assessments in survivorship care. Collectively, these findings extend current literature by integrating longitudinal supplement use data with detailed symptom profiling, offering new insight into how cancer survivors adapt supplement behaviours over time within a survivorship care context.

Strengths and Limitations

Key strengths of this study include its prospective design, focus on three primary tumour locations and detailed symptom characterisation. It is acknowledged that there are limitations to this secondary analysis. Firstly, the use, dosage and frequency of

supplements was self-reported by participants. However, the tool used, a FFQ is a validated questionnaire, widely used in dietetic and nutrition research. The FFQ only facilitated the reporting of up to eight supplements, however only a small proportion of participants reported more than six supplements at baseline and end of study. Harrigan et al. (2021), have reported similar work, with a range of 0 to 23 supplements, with smaller proportions of participants using greater than eight (29). In the LYSA Trial, no data around source of information or reason for use was collected at baseline and end of study using the FFQ. However, this data were likely collected during healthcare consultations as part of the larger intervention. Additionally, causality cannot be inferred from observed associations. Longitudinal data capturing both the rationale behind supplement use and the information sources consulted would enhance understanding of usage patterns.

Clinical and Practical Implications

The need for structured conversations between survivors and healthcare providers is especially important given the potential for supplement-drug interactions, particularly among individuals receiving endocrine therapies or those managing complex symptom profiles. In five international studies, between 21.6% and 46.1% did not consult or disclose their supplement use to their healthcare provider, citing that the physician did not ask or they felt that the physician did not need to know (9,11,16,18,20). Contrastingly, three US and European studies reported between 51.1% and 82.4% disclosed supplement use to their healthcare provider (15,17,19). Concerningly, in a small cohort of US breast cancer survivors, Silver, Goldenberg and Moore (2025) reported that 0% had an accurate list of dietary/herbal supplements documented in electronic medical records (57). In a small qualitative study of thirty healthcare professionals, Kadro et al. (2023) reported that while most expressed

concerns about supplement safety and potential drug-nutrient interactions, they identified barriers to accurate documentation, including time constraints, inconsistent databases, and poor patient communication about supplement use (58). Interestingly in the Irish context, the O'Donovan et al. (2024) study, conducted in a similar cohort, time frame and geographic setting to the LYSA Trial, reported lower supplement use compared with LYSA (34). Notably, supplement information in that study was collected by medics rather than dietitians, as in LYSA, suggesting that discrepancies in reported use may reflect differences in who is collecting the data and how it is collected, rather than true variation in patient behaviour.

Incorporating routine patient-reported outcome measures, as implemented in the LYSA Trial, could be leveraged similarly in clinical practice. A decade ago, qualitative data from patients and HCPs suggested that discussions should focus on what patients are taking and potential supplement risks, and conclude that interventions to enhance communication about dietary supplements should focus on both patient and HCP education (59). Future clinical advancements should include the development of a comprehensive, yet acceptable supplement screening tool that can be used routinely in oncology survivorship care, co-designed with public and patient involvement, as well as healthcare professionals. Studies examining healthcare provider involvement in supplement decisions and interventions aimed at improving communication about complementary therapies are particularly warranted, given the limited data available.

5.7 CONCLUSION

In this secondary analysis of Irish cancer survivors supplement use was high and increased significantly over 12 months, with breast cancer survivors and those with

higher education levels using the greatest number of supplements - particularly vitamin and mineral supplements. Herbal and botanical supplement use also increased over time, though it was not associated with any demographic or clinical factors, underscoring the importance of asking all patients about use. Additionally, supplement use was associated with symptom burden: greater fatigue, hot flashes, and abdominal pain were linked with higher usage, while severe joint pain and reduced libido were linked with lower use. These findings suggest that supplement use is not only shaped by demographic and clinical factors but also by survivors' efforts to self-manage persistent and bothersome symptoms. Collectively, this study provides novel longitudinal evidence on supplement use patterns within an Irish cancer survivorship cohort, demonstrating both changes over time and symptom-linked differences in supplement behaviour. It also highlights how supplement use evolves within the context of survivorship care, an area that remains under-reported in existing literature. These results underscore the vital need for ongoing, structured assessment of supplement use and patterns - integrating symptom evaluations and sources of supplement information - over five to ten years, particularly for those on long-term treatments such as endocrine therapy. Such longitudinal research, combined with routine symptom monitoring and tailored education, is essential to promote safe, patient-centred, and evidence-informed supplement use.

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CHAPTER 6: ALLEVIATING MENOPAUSAL SYMPTOMS? THE PREVELANCE, INFORMATION SOURCE AND PERCIEVED EFFECTIVENESS OF DIETARY AND HERBAL SUPPLEMENTS IN IRISH FEMALE CANCER SURVIVORS AFFECTED BY TREATMENT INDUCED MENOPAUSE

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6.1 ABSTRACT

Background: The number of new cancer cases in Europe is projected to rise substantially over the next two decades, increasing the population of women living with iatrogenic menopause. Iatrogenic menopause arises as a consequence of cancer therapies, including chemotherapy and endocrine treatments, and is often associated with abrupt and severe menopausal symptoms. Many survivors turn to dietary and botanical supplements to manage these symptoms, despite uncertainties regarding their effectiveness and safety. Managing menopausal symptoms is a critical component of survivorship care, yet many women report unmet needs and limited access to evidence-based interventions. Patterns of supplement use, sources of information, and the extent to which women disclose their supplement use to healthcare providers remain poorly understood, particularly in the Irish context. This study aimed to describe the prevalence and patterns of dietary and herbal supplement use among women experiencing iatrogenic menopause; explore perceived effectiveness, identify sources of information; and examine factors influencing disclosure or non-disclosure of supplement use to healthcare providers.

Methods: A cross-sectional study, reported per STROBE guidelines, used a 32-item online questionnaire (adapted from Hauer et al. 2023). The survey was open in Ireland from March to October 2025, with recruitment via social media, cancer centres and charities. Eligible participants were adults, aged over 18 years assigned female at birth with a current or prior cancer diagnosis experiencing menopausal symptoms, with access to the internet. Ethical approval was obtained from the Clinical Research Ethics Committee of Cork Teaching Hospitals. Data were analysed descriptively in R (v4.5.0), and open-text responses were thematically analysed using Braun and Clark's framework (2006).

Results: Of 108 respondents that consented to the study, 75 met the inclusion criteria and were included in the final analysis. Most were aged 30-59 years (93.3%), employed (73.3%), and held third-level education (84%). Breast cancer was the predominant diagnosis (85%, n = 64), and 70% had received or currently prescribed endocrine therapy. Over half (57%, n = 43) were postmenopausal, with 79% (n = 59) attributing symptoms to iatrogenic menopause. The most severe symptoms were low libido (47%), insomnia (31%), and vaginal dryness (27%). Supplement use was common: 67% used vitamins/minerals and 47% used herbal products, with 39% using both. Magnesium, vitamin D, and calcium were the most frequent supplements; melatonin, Asian Mushrooms, and turmeric or curcumin were the leading herbal products. Of participants who reported herbal supplement use (n = 35) around 20% rated them as very effective. Similarly of those who reported vitamin and mineral use (n = 50) 30% rated them as very effective. Information sources included the internet/social media (41%) and healthcare professionals (14%) for herbal products, and physicians (35%) and online media (19%) for vitamins/minerals. Only 53% disclosed supplement use to their medical team. Reported reasons for disclosure included safety and trust; whereas non-disclosure reflected limited opportunities, perceived clinician disinterest, and confidence in self-directed research.

Conclusion: Supplement use for iatrogenic menopausal symptoms is widespread among cancer survivors, often guided by online information with moderate perceived benefit. Limited disclosure and professional guidance highlight the need for better communication, evidence-based education, and greater dietitian involvement. Future research should assess supplement safety, efficacy and develop practical tools to support informed survivorship care.

6.2 INTRODUCTION

The projected trend of new cancer cases in females, excluding non-melanoma skin cancer, from 2022 to 2045 will increase by 55.5% (1). Advances in early detection and treatment mean that the number of individuals living beyond a cancer diagnosis is growing globally. As survivorship increases, attention to long-term health and supportive care needs become critical.

A key, yet often overlooked, aspect of survivorship care for female cancer survivors is iatrogenic menopause - a medically induced menopause arising from cancer treatments such as chemotherapy and endocrine therapy which may be permanent or temporary. Menopausal status prior to cancer treatment and therapeutic agents used, such as chemotherapy and endocrine therapy, impact the specific symptoms and clinical challenges faced in iatrogenic menopause (2). Symptoms caused by iatrogenic menopause can be more severe than that of a "natural" menopause, due to the abrupt decrease of oestrogen (3).

In their aptly titled systematic review "*It's not over when it's over…*", Harrington and colleagues highlighted that cancer survivors, including breast and gynaecologic, can experience symptoms for more than 10 years following treatment (4). These symptoms include cognitive limitations, depression and anxiety, fatigue, physical limitations, pain and sexual dysfunction (4). Despite the significant clinical and global impact, accessible literature quantifying this burden remains limited (3). Even outside of the context of iatrogenic menopause, 80%-90% of women will experience menopausal symptoms, with approximately one-third reporting symptoms severe enough to significantly impact daily quality of life (5). This underscores the potential magnitude

of symptom burden among women undergoing a sudden, iatrogenic menopausal transition.

This considerable symptom burden highlights a significant unmet need in survivorship care, which may help explain the growing reliance on complementary strategies, including the use of vitamin, mineral, and herbal supplements (6). International oncology guidelines discourage the use of vitamin/mineral and herbal supplements in cancer survivors, citing limited evidence for their safety, efficacy and use outside of a diagnosed deficiency. Despite these guideline recommendations, supplement use, particularly in females cancer survivors, remains highly prevalent (7). Many survivors turn to supplements in an attempt to alleviate treatment-related symptoms, including those associated with endocrine therapies (8–13), however few quantify the motivations or perceived effectiveness of supplements in alleviating symptoms, particularly in those impacted by iatrogenic menopause. Studies have reported that up to 50% of women use non-pharmacologic therapies to manage menopausal symptoms, many of which are not supported by high quality evidence (14,15). This reliance on non-pharmacological approaches may be especially prominent among cancer survivors for whom hormone replacement therapy (HRT) is contraindicated due to recurrence risk, such as those with hormone receptor-positive breast cancer (16). The disclosure of supplement uses to medical teams reported in the literature varies, with inconsistent results ranging from ~20% to ~50% of cancer survivors (9,10,12,13,17–20).

Whilst data regarding general supplement use in cancer survivors will well defined, there is limited data on supplement use among female cancer survivors managing iatrogenic menopause, including sources of information and perceived effectiveness. Furthermore, data are lacking on the factors influencing patients' disclosure or non-

disclosure of supplement use during routine oncology consultations. With projected increases in breast, cervical and endometrial cancer incidence in Ireland relative to Europe (21) understanding these is essential. Investigating these factors can inform evidence-based practice and support clinical decision-making among healthcare professionals and multidisciplinary teams as care for iatrogenic menopause in cancer survivorship is expanding.

6.3 AIMS AND OBJECTIVES

The aim of this cross-sectional study was to describe the proportion of female cancer survivors using dietary and botanical supplements to alleviate iatrogenic menopause symptoms; describe patterns of supplement use; the perceived effectiveness of these supplements; and female cancer survivors' primary information source. While the primary focus was quantitative, qualitative data were analysed to explore participant-reported factors influencing disclosure or non-disclosure of supplement use to medical teams.

6.4 METHODS AND MATERIALS

This study is reported using the Checklist for Reporting Cross-sectional Survey Studies (CROSS) to enhance transparency of survey design, administration and reporting (22).

6.4.1 Study Design

This cross-sectional survey study was conducted using an anonymous, online questionnaire hosted on Qualtrics. The survey was adapted with permission from Hauer et al. (2023), which examined dietary supplement use in breast cancer survivors (23) . Adaptations were made to ensure relevance to an Irish cancer survivor

population and to include additional domains relating to menopausal symptom burden, supplement use for symptom management, and information sources. The final instrument consisted of 32 questions across four domains:

- Demographic and clinicopathologic characteristics
- Herbal supplement use
- Vitamin and mineral supplement use
- Sources of information and disclosure behaviours

The survey included a combination of multiple-choice, Likert-scale, and open-text questions. Likert scales were used to assess menopausal symptom severity and perceived effectiveness of supplements. Open-text responses explored motivations for supplement use and reasons for disclosure or non-disclosure to healthcare professionals.

6.4.2 Questionnaire Development and Content Validity

The survey instrument was based on a previously validated questionnaire (Hauer et al., 2023) and was adapted through iterative discussion among the research team to ensure clinical relevance and comprehensiveness for a mixed cancer survivor population experiencing iatrogenic menopause.

Prior to deployment, the questionnaire was reviewed for content clarity, clinical relevance, and face validity by the research team and oncology dietetic specialists. Minor refinements were made to wording and structure. Due to the observational and exploratory nature of the study, formal psychometric validation was not undertaken; however, the instrument was modelled on previously published and widely used survey items in cancer survivorship research.

6.4.3 Setting and Survey Administration

The survey was hosted online using Qualtrics and was available from 14th March 2025 to 2nd October 2025. Recruitment was conducted using convenience sampling. Participants were recruited through multiple channels, including social media platforms (Instagram, X, BlueSky); newsletters distributed by cancer organisations; digital and printed flyers; passive dissemination via cancer centres and support organisations. No direct clinical recruitment occurred. Participation was voluntary, anonymous, and completed online.

6.4.4 Study Population and Eligibility Criteria

Participants were eligible for inclusion if they were assigned female sex at birth, aged 18 years or older, residing in the Republic of Ireland, had a current or previous diagnosis of any cancer, and self-reported experience of iatrogenic menopause. Eligibility additionally required the ability to read and understand English and access to the internet, as the survey was administered online. Individuals who did not provide informed consent or were unwilling to participate were excluded.

Menopausal status was determined by participant self-report using standardised lay descriptions of premenopausal, perimenopausal, and postmenopausal stages provided within the survey instrument. This approach was used to facilitate participant understanding in the absence of clinical verification.

6.4.5 Sample Size

Reported rates of chemotherapy-induced amenorrhoea and premature ovarian insufficiency vary widely in the literature, ranging from 15% to 94%, depending on differences in definitions, patient age, treatment regimens, and duration of follow-up

(24). Due to the substantial heterogeneity, and the scarcity of age-stratified data, there is no reliable effect size or expected event rate to inform a conventional sample size calculation. Given these limitations and the exploratory nature of the study a formal sample size calculation was not feasible. Accordingly, the study was designed to generate preliminary, hypothesis-generating data that will inform future fully powered research.

6.4.6 Survey Administration Integrity and Data Quality Assurance

To minimise duplicate entries, Qualtrics settings were configured to restrict multiple submissions from the same device where possible. In addition, IP address monitoring and survey completion time screening were used during data cleaning to identify potential duplicate or automated responses. No evidence of duplicate entries was identified following cleaning procedures.

6.4.7 Data Processing and Cleaning

Data were exported from Qualtrics and imported and cleaned in R (version 4.5.0) for analysis (25). Column names were standardised, and ineligible or incomplete records were removed. Multi-response items, (e.g. treatments received) were collected as comma-separated fields and were separate binary variable to retain one row per participant. Variables were grouped thematically: Demographic and Clinicopathologic variables (age, sex, education, employment, cancer diagnosis and type, treatments received); Menopausal Symptom Severity; Herbal and Vitamin/Mineral Supplement Use; Perceived Effectiveness of Supplements; Sources of Information; Disclosure to Medical Teams. Participants prescribed HRT were not excluded from analysis due to the nature and symptomology of an iatrogenic menopause.

6.4.8 Statistical Analysis

Descriptive statistics were calculated using counts and percentages. For multi-response items, each selected option was treated as a separate category and counted individually. All analyses were conducted in R to ensure reproducibility. A thematic analysis approach was used to explore reasons for disclosure/non-disclosure of supplement use to healthcare professionals, following the framework outlined by Braun and Clarke (2006) (26). All responses were read multiple times to ensure familiarity with the data. Initial codes were generated inductively, capturing recurring ideas and meanings across the dataset. Codes were then grouped into broader themes and subthemes that reflected shared patterns of experience (26). Codes were reviewed by two researchers, with one researcher conducting the analysis and a second reviewing the themes and checking against the original qualitative responses.

6.4.9 Ethical Approval and Data Protection

Ethical approval was obtained from the Clinical Research Ethics Committee of the Cork Teaching Hospitals [CREC ECM 4 (mm) 05/12/2023 & ECM 3 (nnnn) 11/03/2025] and the survey was conducted using Good Clinical Practice Guidelines, and in accordance with the Declaration of Helsinki. All participants provided informed consent prior to survey completion. Data were collected anonymously, securely stored, and accessed only by the research team. No identifiable information was collected at any stage.

6.5 RESULTS

A total of 108 participants consented to the survey, of whom 75 met the inclusion criteria and were included in the final analysis. A true response rate could not be calculated due to the open recruitment strategy via social media and organisational

dissemination, which did not allow estimation of total survey viewership. Participants were excluded for being male (n = 4); not consenting to the survey (n = 4); not having a cancer diagnosis (n = 9); or not completing the survey in full (n = 16). No additional stage-specific non-response data were available within Qualtrics export, and no duplicate or automated responses were identified following IP and completion-time screening during data cleaning

6.5.1 Demographic and Clinicopathological Characteristics

Over 80% of participants were between the ages of 30 – 59 years and 57.3% reported completed third level education (Table 6.1). Most participants (73.3%) were in paid employment, with 24% working between 32 – 40 hours per week. Geographically, responses came from nineteen of the thirty-two counties in Ireland, with an increased number of responses from Dublin (29.3%) and Cork (16%), reflective of the population density.

As shown in Table 6.1, breast cancer accounted for most diagnoses (85.3%), with ovarian cancer comprising 5.3%. Most participants (76%) indicated a curative treatment intent. In terms of time since diagnosis, 38.7% reported 1 - 2 years since diagnosis. In relation to anti-cancer treatments, 90.6% received surgery, 77.2% received chemotherapy and 70.6% received radiotherapy. Seventy percent of participants reported receiving endocrine therapy, with 65.3% still receiving the adjuvant therapy at the point of survey completion. Most participants were prescribed an aromatase inhibitor (50.7%), with a smaller proportion prescribed a selective oestrogen receptor modulator (18.7%).

Table 6.1: Demographics and Clinicopathologic Characteristics (n = 75)

Characteristic	N	%
Demographic		
Sex		
Female	75	100
Age (in years)		
30-39	7	9.3
40-49	32	42.7
50-59	31	41.3
60-69	5	6.7
Province of Residence		
Leinster	42	56
Munster	28	37.3
Connacht	3	3.9
Ulster	2	2.6
Paid Employment		
Yes	55	73.3
No	20	26.7
Hours Working Per Week		
0 - 8 hours	24	32
8 - 16 hours	2	2.7
16 - 24 hours	13	17.3
24 - 32 hours	12	16
32 - 40 hours	18	24
40 + hours	6	8
Education Level		
No education	0	0
Primary level education	0	0
Second level education (junior certificate, leaving certificate, technical or vocational qualification)	12	16
Third level education (Bachelor's degree, postgraduate certificate or diploma)	43	57.3
Third level education (Postgraduate degree)	20	26.7
Clinicopathologic		
Primary Tumour Location		
Breast	64	85.3
Ovarian	4	5.3
Non-Hodgkin Lymphoma	2	2.7

Skin	2	2.7
Other *	3	4
Treatment Intent ~		
Curative	57	76
Metastatic	14	18.7
I'm not sure	3	4
Years since Diagnosis		
Less than 1 year ago	9	12
1 - 2 years ago	29	38.7
3 - 5 years ago	10	13.3
5 - 10 years ago	18	24
More than 10 years ago	9	12
Anti-Cancer Treatments to Date ^		
Surgery	68	90.6
Chemotherapy	58	77.2
Radiotherapy (Internal Beam and External Beam)	53	70.6
Endocrine Therapy	53	70.7
Immunotherapy	20	26.7
Current Anti-Cancer Treatments Received ^		
Endocrine Therapy	49	65.3
Finished Treatment (In remission)	16	21.4
Chemotherapy	5	6.7
Radiotherapy (Internal Beam and External Beam)	5	6.7
Immunotherapy	4	5.3
Surgery: Planned	3	3.9
On a break from treatment	1	1.3
Endocrine Therapy		
Anastrozole (Arimidex)	21	28
Tamoxifen	14	18.7
Letrozole (Femora)	9	12
Exemestane (Aromasin)	8	10.7
Unspecified Endocrine Therapy	2	2.7
Menopausal Status		
Post-menopausal	43	57.3
I'm having menopausal symptoms, but I am not sure what stage of the menopause I am in.	23	30.7
Peri-menopausal	7	9.3
I have no menopausal symptoms, and I am unsure of what stage I am in.	1	1.3
Pre-menopausal	1	1.3
Iatrogenic Menopause ~		
Yes	59	78.7

No	10	13.3
Not sure	5	6.7
Hormone Replacement Therapy ~		
No	64	85.3
Yes	10	13.3

^ Variables "Anti-Cancer Treatments to Date" and "Current Anti-Cancer Treatments Received" are multi-response, so percentages may sum >100%

* Other includes: Leukaemia (n = 1), Pancreatic (n = 1) and Renal (n = 1)

~ N = 1 participant did not disclose

6.5.2 Self-Reported Menopausal Symptoms

Of note, 30.7% reported that they were unsure of what stage of menopause they were in, despite having symptoms, and 57.3% reported a post-menopausal status. Only 13.3% reported hormone replacement therapy use, with 78.7% reporting that their symptoms were a result of iatrogenic menopause.

As described in Figure 6.1, participants reported the severity of common menopausal symptoms. The most reported severe menopausal symptom was low sex drive (46.7%), followed by insomnia (30.7%) and vaginal dryness (26.7%). Symptoms of moderate severity included fatigue (58.7%), focus (54.7%), memory (48%) and hot flashes (44%). Common symptoms of mild severity included skin dryness (46.7%), headaches (42.7%), irritability (38.7%), and depression (38.7%).

6.5.3 Supplement Use

Of participants, 77.3% reported supplement use. Participants reported using herbal supplements (46.7%) and vitamin/mineral supplements (66.7%) to alleviate menopausal symptoms, with 38.7% using a combination of both categories of supplements. Approximately one fifth (22.7%) reported using no supplements, 40% reported using between 1 to 4 supplements of any category, 24% used between 5 to 8 supplements and 13.3% reported using 9 to 15 supplements. In relation to herbal

supplements, 38.6% used between 1 to 2 supplements and 13.3% reported using between 3 to 5 supplements. Total supplement count was higher in participants using vitamin and mineral supplements, with 46.7% using between 1 to 4 supplements and 25.2% using between 5 to 10 supplements.

The most commonly reported herbal and botanical supplement was melatonin (17.3%), followed by Asian Mushrooms (14.7%) and Turmeric/Curcumin (13.3%) (Table 6.2). In relation to vitamin and mineral supplements, 50.7% reported magnesium use, 45.3% reported vitamin D use, and 40% reported calcium use (Table 6.2).

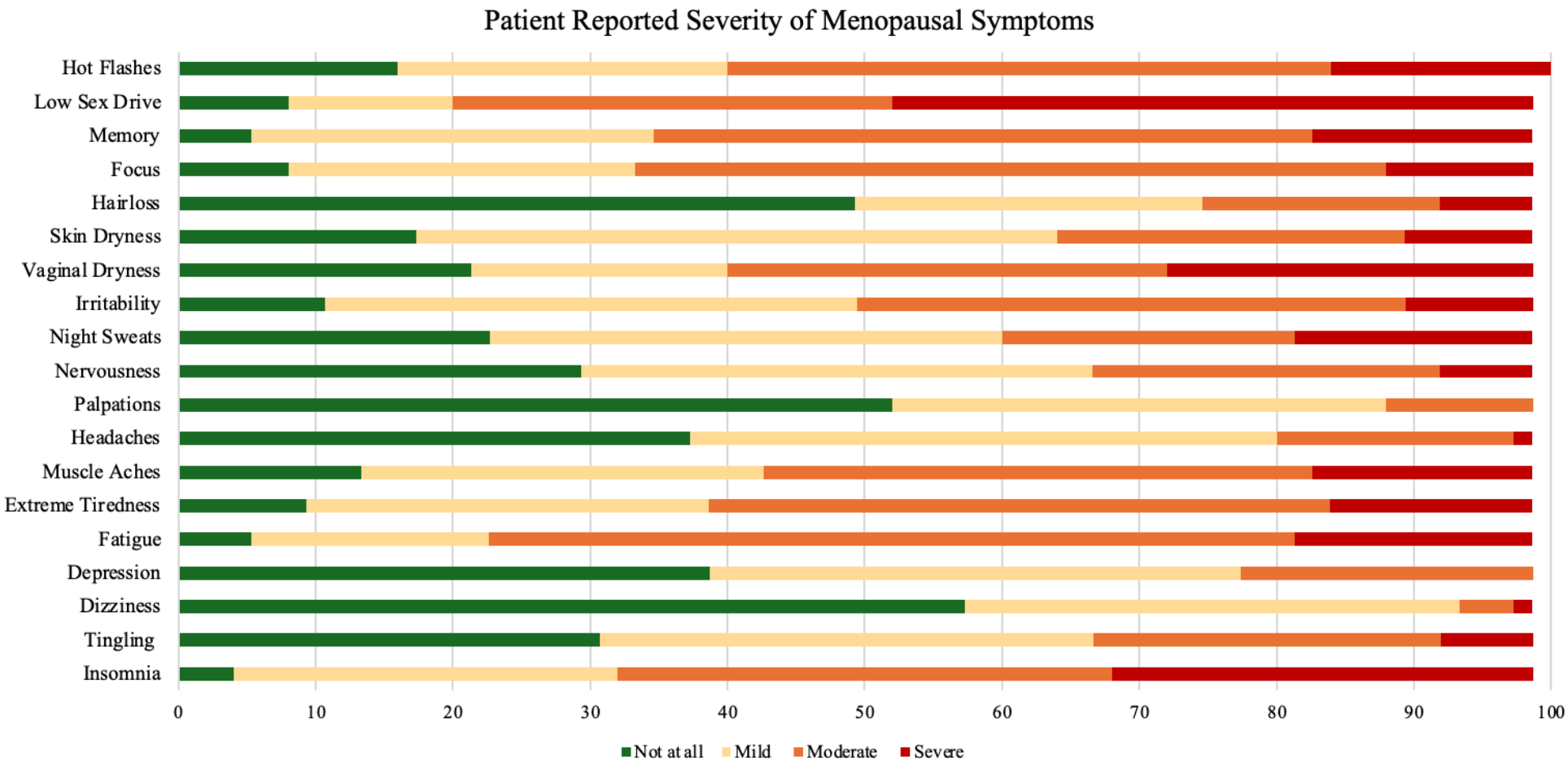


Figure 6.1. Patient Reported Severity of Menopausal Symptoms

6.5.4 Use of Supplements for Symptom Relief and Patient Reported Perceived Effectiveness

Participants reported a range of symptoms that supplements were being used to alleviate [Supplementary Tables 6.2 and 6.3]. These included general health symptoms and those associated with iatrogenic menopause.

Tart cherry was reported to be used for bone pain (3%), joint pain (< 2%), fatigue (< 2%), and insomnia (< 2%), whilst ashwagandha was used for anxiety (4%), stress (3%) and sleep (1%).

Asian Mushrooms (e.g. Lion's Mane) was reported to be used for cognitive symptoms (5%), immunity (3%), night sweats (< 2%) and overall menopausal symptoms (3%).

Calcium was reported for bone health by all participants who used it (38.7%), whilst magnesium was used to alleviate insomnia (30.7%), muscle pain (8%), joint pain and cramps (both 6.7%) [Supplementary File 6.3].

Omega 3 Fish Oils, containing eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) only, were used to alleviate cognitive symptoms (13.3%), joint pain (6.5%), with only 2.7% having reported its use as a supplement to their diet. B Vitamins were reported to be used for general health (8%) and cognitive symptoms (4%), whilst Vitamin C was reported to be used immunity (6.7%), general health (4%) and bone health (2.7%).

Vitamin D was used to support bone health (37.3%), cognitive symptoms (6.7%) and immunity (4.0%). Vitamin K was reported to be used to aid the absorption of Vitamin D (2.7%) and for bone health, general health and heart health (all 1.3%).

Table 6.2: Patient Reported Supplement Use (n = 75)

Supplement	N	%
Herbal Supplements		
Melatonin	13	*17.3%*
Asian Mushrooms (e.g Lion's Mane)	11	*14.7%*
Turmeric or Curcumin	10	*13.3%*
Evening Primrose Oil	7	*9.3%*
Collagen	7	*9.3%*
Ashwagandha	6	*8%*
Tart Cherry	4	*5.3%*
Sage	4	*5.3%*
Other *	10	*13.3%*
Vitamin and Mineral Supplements		
Magnesium	38	*50.7%*
Vitamin D	34	*45.3%*
Calcium	30	*40%*
Omega 3 Fish Oil (containing EPA & DHA only)	16	*21.3%*
Fish Oil - such as cod liver oil or fish oil blend	12	*16%*
Multivitamin	12	*16%*
Probiotic (such as a sachet or capsule)	12	*16%*
Vitamin C	10	*13.3%*
Zinc	7	*9.3%*
Iron	6	*8%*
Glucosamine	5	*6.7%*
Vitamin B Complex	5	*6.7%*
Menopause Specific-Multivitamin	4	*5.3%*
Vitamin B7 (Biotin)	4	*5.3%*
Vitamin K	4	*5,3%*
Vitamin B6	3	*4%*
Other ^	6	*8%*

** Other herbal supplements include: Soy isoflavones (n = 2), maca root (n = 2), slippery elm bark (n = 1), rose hip oil (n = 1), red yeast rice (n = 1), red clover (n = 1), ginseng (n = 1), echinacea (n = 1)*

^ Other vitamin mineral supplements include: selenium (n = 2), Vitamin E (n = 2), Vitamin A (n = 1), Vitamin B3 (n = 1)

Abbreviations: EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid.

Of herbal supplements reported, 15% were perceived to be not effective at all in alleviating menopausal symptoms overall, whilst 20.5% were perceived to be very effective in alleviating symptoms. Similarly, of vitamin and mineral supplements reported, 9.7% were perceived to be not effective at all in alleviating menopausal symptoms, whilst 30.3% were perceived to be very effective in alleviating menopausal symptoms.

6.5.5 Sources of Information for Supplement Use

Participants reported their most common source of information for each individual supplement (Table 6.3). The internet or social media was the most common source of information for herbal supplements (40.5%), followed by other healthcare professional (e.g. nurse or pharmacist) (13.5%), other female cancer survivors, family and/or friends or primary consultant/general practitioner (all 12.2%).

Looking at information sources of individual herbal supplements, the internet and social media was most used for Asian Mushrooms (54.55%), followed by other healthcare professionals, e.g. nurse or pharmacist (27.27%). Information on ashwagandha use was sourced from internet or social media (50%), followed by other female cancer survivors (33.3%). Soy isoflavone, ginseng, maca root and red clover information was solely sourced from the internet or social media. Slippery elm bark use information was solely sourced from the primary consultant or general practitioner, whilst red yeast rice use was sourced from family and/or friends and rose hip oil from other cancer survivors (all 100%). Turmeric or Curcumin was the only herbal supplement that had a registered dietitian as a source (10%).

The most common source of information for the use of vitamin and mineral supplements was primary consultant or general practitioner (35.1%), followed by the internet or social media (18.5%) and other healthcare professionals, e.g. nurse or pharmacist (15.3%). A registered dietitian was reported as a source of information for only 2.3% of occurrences relating to vitamin or mineral supplements.

Looking at sources of information for individual vitamin and mineral supplement use, primary consultant/general practitioner was cited as the main source of information for calcium (73.33%) and vitamin D (65.71%) (Table 6.3). A nutritional

therapist/nutritional coach was the main source of information for vitamin A (50%), vitamin B1 (100%), vitamin B3 (50%), vitamin B6 (50%), vitamin B7 (40%), vitamin B9 (100%), vitamin B Complex (33.33%), and vitamin E (33.3%). A registered dietitian was cited as a source of information for calcium (3.33%), fish oil (8.33%), magnesium (2.63%), probiotic (8.33%), and zinc (12.5%). Information sources for menopause specific multivitamins included other healthcare professionals (e.g. nurse and pharmacist) (50%), internet and social media (25%) and family and/or friends (25%), whilst the most common information source for a multivitamin was other healthcare professional (e.g. nurse and pharmacist) (33.33%), and health store assistant (25%). The primary information sources for glucosamine were primary consultant/general practitioner (60%), other healthcare professional, e.g. nurse and pharmacist (20%), and internet and social media (20%). Probiotic sources of information were primarily from internet and social media (41.67%).

Table 6.3: Patient Reported Primary Source of Information for Supplements

Supplement ^	Primary Source of Information (%) *
Vitamin Mineral Supplement	
Calcium	Primary consultant/general practitioner (73.3%)
Fish Oil - such as cod liver oil or fish oil blend	Primary consultant/general practitioner (25%) Internet or social media (25%)
Glucosamine	Primary consultant/general practitioner (60%)
Iron	Primary consultant/general practitioner (33.3%) Internet or social media (33.3%)
Magnesium	Primary consultant/general practitioner (36.8%)
Menopause Specific-Multivitamin	Other healthcare professional (50%)
Multivitamin	Other healthcare professional (33.3%)
Omega 3 Fish Oil (containing EPA & DHA only)	Internet or social media (37.5%)
Probiotic (such as a sachet or capsule)	Internet or social media (41.7%)
Selenium	Other healthcare professional (50%) Health store assistant (50%)
Vitamin B Complex	Other healthcare professional (33.3%) Family and/or friends (33.3%) Nutritional therapist or nutritional coach (33.3%)
Vitamin B6	Nutritional therapist or nutritional coach (50%)
Vitamin B7 (Biotin)	Nutritional therapist or nutritional coach (40%)
Vitamin C	Internet or social media (36.4%)
Vitamin D	Primary consultant/general practitioner (65.7%)
Vitamin E	Primary consultant/general practitioner (33.3%) Family and/or friends (33.3%) Nutritional therapist or nutritional coach (33.3%)
Vitamin K	Internet or social media (80%)
Zinc	Family and/or friends (25%)
Herbal Supplement	
Ashwagandha	Internet or social media (50%)
Asian Mushrooms (e.g Lion's Mane)	Internet or social media (54.6%)
Collagen	Internet or social media (28.6%) Family and/or friends (28.6%)
Evening Primrose Oil	Primary consultant/general practitioner (28.6%) Other female cancer survivors (28.6%) Internet or social media (28.6%)
Melatonin	Primary consultant/general practitioner (38.5%)
Sage	Internet or social media (75%)
Tart Cherry	Other female cancer survivors (75%)
Turmeric or Curcumin	Internet or social media (70%)

^ Supplements with >3 users reported

** Percentages are expressed as the number of participants reporting those supplements*

Abbreviations: EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid.

6.5.6 Disclosure of Supplement Use to Healthcare Professionals

Approximately half of participants (53.3%) reported disclosing supplement use to their medical team. A brief reflexive thematic analysis identified key themes influencing disclosure or non-disclosure decisions (Table 6.4).

Four themes underpinned why participants chose to disclose supplement use.

1. Safety and Interaction Concerns

Disclosure frequently stemmed from a desire to ensure safety and avoid potential interactions between supplements and cancer therapies. Participants expressed uncertainty about what was appropriate after cancer treatment and often sought reassurance from multiple healthcare professionals. As one participant explained, *"To ensure that they were safe to take after the type of cancer I had."* Subthemes included checking for drug-supplement interactions, particularly when taking an endocrine therapy or adjuvant treatments; fear of negative effects or cancer recurrence, prompting heightened caution; and double-checking with multiple professionals to validate safety.

2. Managing or Alleviating Symptoms, Desire for Holistic and Natural Support

Participants disclosed supplement use when they were using products to manage treatment-related or menopause-associated symptoms, including hot flushes, sleep disturbance, and concerns about bone health. Supplements were sometimes viewed as alternatives when HRT was contraindicated. As one participant described, *"For side effects from cancer treatments, induced menopause and osteoporosis."* Subthemes including managing treatment side effects such as sleep disturbances or fatigue; bone health, especially in relation to osteoporosis; and alternatives to HRT, in instances

where it is contraindicated; natural products perceived as gentler or safer; and seeking complementary approaches aligned with personal wellbeing philosophies.

3. Professional Guidance and Trust

Disclosure was prompted when healthcare professionals had previously recommended supplements, or when participants wished to maintain transparent communication regarding self-management strategies. One participant noted, *"Oncologist advised melatonin and vitamin D."* Subthemes included following oncologist or doctor recommendations for specific supplements; disclosure for treatment alignment, ensuring self-management practices did not conflict with care plans; recognising limitations in medical training yet still valuing clinician oversight.

4. Autonomy and Self-Directed Research

Several participants framed themselves as active agents in their care, conducting independent research into supplement quality or suitability. Disclosure occurred to align their decisions with cancer treatment plans while maintaining autonomy. As one participant stated, *"I do a lot of research into what is absorbable."* Subthemes included independent learning and evidence seeking, such as researching supplement quality, forms or absorption; and balancing medical advice with personal beliefs, integrating research with clinician input.

Four themes captured why participants chose not to disclose supplement use.

1. Lack of Perceived Relevance

Some participants did not view supplement use as clinically relevant or necessary to discuss, particularly if symptoms were manageable or supplements had been taken long before diagnosis. One participant indicated, *"I didn't feel I needed them."*

Subthemes included viewing supplements as unnecessary or providing limited benefit; managing symptoms independently, without supplements or clinical guidance; limited understanding of supplements, leading to reduced confidence in raising the topic; and uncertainty around discussions or expectations of clinician involvement.

2. Healthcare Professionals Attitudes and Knowledge

Non-disclosure was also driven by perceptions that clinicians were uninterested or sceptical about supplements, discouraging conversation. One participant remarked, *"I would not bother asking them as they would just be dismissive."* Subthemes included the belief of clinician scepticism, reducing motivation to disclose; and the perception that supplements were outside medical remit, especially in oncology. Furthermore, non-disclosure was also shaped by treatment burden and fragmented service pathways, with some participants feeling overwhelmed or unsure which clinician was responsible for such discussions. As one participant expressed, *"I am going through treatment at the moment… I can't take in more info."* Subthemes included being overwhelmed during active treatment, making supplement discussions secondary; and fragmented care pathways, including discharge from relevant services or unclear clinical responsibility.

3. Practical Barriers

Non-disclosure was shaped by treatment burden and fragmented service pathways, with some participants feeling overwhelmed or unsure which clinician was responsible for such discussions. As one participant expressed, *"[I] have not had an appointment where it was discussed."* Subthemes included being overwhelmed during active treatment, making supplement discussions secondary; and fragmented care pathways, including discharge from relevant services or unclear clinical responsibility. Many

participants described a lack of suitable opportunities to raise supplement use during clinical appointments, which were often focused exclusively on cancer-related issues. Subthemes included treatment-focused consultations that prioritised cancer outcomes; and difficulty contacting clinicians outside scheduled visits. Several participants described care that focused narrowly on cancer surveillance, with limited attention to menopause or wider wellbeing, reducing the perceived relevance of discussing supplements. One stated, *"Mention menopause and it is glossed over."* Subthemes included concerns about menopause being minimised, reducing relevance of supplement discussions; pharmaceutical focused advice, with little mention of non-pharmacological options; and perceived lack of clinician training in menopause management.

4. Autonomy and Self-Directed Research

A small group, particularly those with a healthcare or scientific background, preferred to rely on their own knowledge and appraisal of evidence rather than seeking clinical input. As one participant explained, *"Because I am a pharmacologist and do my own research."* Subthemes included balancing medical advice with personal beliefs and independent learning and research.

Table 6.4: Thematised Reasons for Disclosure and Non-Disclosure of Supplements Use to Healthcare Professionals

Category	Main Theme	Subthemes	Illustrative Quotes
Reasons for Disclosure	Safety and Interaction Concerns	• Checking for drug/supplement interactions • Fear of negative effects or recurrence • Double-checking with multiple professionals	"To ensure that they were safe to take after the type of cancer I had." "Wanted to ensure safe to take with treatment." "Scared to use supplements post cancer diagnosis." "I take nothing before double checking with oncology nutritionist."
	Managing or Alleviating Symptoms, Desire for Holistic or Natural Support	• Managing side effects from treatment or induced menopause • Bone health and hormonal effects • Alternatives to HRT • Preference for natural products • Seeking complementary approaches	"For side effects from cancer treatments, induced menopause and osteoporosis." "I want to take care of my bones and prevent osteoporosis." "As I can't take HRT, I've spoken about natural remedies." "To try and alleviate symptoms by using more natural products." "Hoped for a natural ease/help with symptoms." "To see if anything would help."
	Professional Guidance and Trust	• Doctor or oncologist recommendations • Disclosure for transparency • Perceived limitations in medical advice	"Oncologist advised Melatonin and Vitamin D." "I will mention it in case it interferes with treatment plans." "Doctors have very little training in supplements or nutrition."
	Autonomy and Self-Directed Research	• Independent learning and research • Balancing medical advice with personal beliefs	"I do a lot of research into what is absorbable." "Try to use more natural or activated forms of nutrients." "I resumed supplements post-treatment with exceptions."
Reasons for Non-Disclosure	Lack of Perceived Relevance	• Did not feel supplements necessary • Symptoms manageable without them • Didn't know much about supplements • Unsure what to ask or expect	"I didn't feel I needed them." "I've seen little evidence of the benefits… I just deal with symptoms." "Was already taking them at the time of cancer diagnosis." "Never thought about it." "I don't know much about supplements." "It's not something my doctors have ever approached with me."
	Healthcare Professional Attitudes and Knowledge	• Doctors uninterested or sceptical about supplements • Feel discussion is outside their remit	"They are not interested. They discuss the cancer piece." "My GP does not approve of supplements."

	• Focus only on cancer, not wellbeing or menopause • Advice limited to medications, not supplements	"I would not bother asking them as they would just be dismissive." "Doctors are sceptical." "Neither my GP nor consultant has any interest in discussing." "They are not interested in alternative/supportive healing." "Mention menopause and it is glossed over." "They didn't want to know about menopause." "I have discussed menopausal symptoms, but only antidepressant and Vagifem were offered." "They haven't mentioned anything about supplements." "I do not feel my GP is well informed about menopause."
Practical Barriers	• No suitable appointments • Overloaded or treatment-focused consultations • Hard to contact healthcare providers • Too much going on with active treatment • Prioritising other care needs • Fragmented care or discharge from relevant services	"Have not had appointment where it was discussed." "Appointments are only breast cancer related." "Too hard to contact." "Not had the opportunity to discuss." "They are too busy." "I am going through treatment at the moment… haven't spoken about menopause medication as I can't take in more info." "Haven't met my new oncologist yet, only 8 weeks out from surgery." "Appointments are only breast cancer related; colorectal and gynae have discharged me." "Apart from DEXA advice, not much discussion in GP setting."
Autonomy and Self-Directed Research	• Independent learning and research • Balancing medical advice with personal beliefs	"I do a lot of research into what is absorbable." "Try to use more natural or activated forms of nutrients." "I resumed supplements post-treatment with exceptions."

6.6 DISCUSSION

Whilst supplement use in cancer survivorship is well documented, this study sought to explore supplement use for symptom relief among female cancer survivors affected by iatrogenic menopause, with a particular focus on prevalence, disclosure practices, perceived effectiveness, information sources, and factors influencing communication with healthcare professionals. Supplement use was highly prevalent in this cohort, with nearly half of participants reporting herbal supplement use and approximately two-thirds reporting vitamin or mineral supplementation. Despite this high level of use, only 53% of participants disclosed supplement use to their medical team. Qualitative findings revealed that disclosure was primarily motivated by safety concerns, symptom management needs, and trust in clinicians, whereas non-disclosure was influenced by limited opportunities for discussion, perceived disinterest, fragmented survivorship care, and systemic barriers. Together, these findings suggest the widespread reliance on supplements for symptom management and persistent gaps in communication within survivorship care.

Prevalence and Patterns of Supplement Use

Supplement use was highly prevalent in this cohort, with 77.3% of participants reporting use of at least one supplement, consistent with rates reported in previous cancer survivorship studies. Early work by Mahady et al. (2003) reported that 79% of respondents were dietary and herbal supplement users, with 48.4% using three or more supplements (27). These findings also resonate with recent Irish literature from O'Donovan et al. (2024) who reported 84% of breast cancer survivors used supplements (28), although this current study extends these findings by focusing on iatrogenic menopausal symptom relief and integrating patient-reported motivations.

Poly-supplementation was a prominent feature of supplement use in this cohort, reflecting participants' efforts to address multiple concurrent symptoms, with 40% using 1 – 4 supplements and 24% using between 5 – 8 supplements. This finding aligns with existing literature indicating that cancer survivors frequently use multiple supplements simultaneously. Previous studies have cited mean intakes of 3.1 ± 2.4 individual supplements, with some breast cancer survivors using up to 23 supplements (8,23,27,29).

In the present study, vitamin D and calcium were the most commonly used supplements, reflecting guideline recommendations from American Society of Clinical Oncology (30) and European Society for Medical Oncology (31) for bone health in breast cancer survivors receiving endocrine therapy. General health maintenance was cited as a reason for supplement use in twelve vitamin and mineral supplements, consistent with wider literature on supplement use for cancer survivors (8,9,11,17,20,32,33).

In contrast, herbal supplement use was more heterogeneous and raises great safety concerns. Five herbal supplements reported collectively by 26.7% of participants, namely ashwagandha, ginseng, maca root, slippery elm bark, and turmeric/curcumin, have known or potential interactions with adjuvant endocrine therapies. Several of these supplements, including maca root, ashwagandha, and turmeric/curcumin, have also been identified by the European Commission as substances of potential concern with respect to human health (34). These findings underscore the importance of routine screening for supplement use in oncology follow-up care, particularly in the context

of poly-supplementation, given the potential for drug-supplement interactions and variability in evidence support efficacy.

Qualitative findings suggest that poly-supplementation was often driven by autonomy, self-directed research, and a desire for holistic approaches to symptom management. Participants frequently described experimenting with multiple products to manage complex and overlapping symptoms, highlighting the need for clearer clinical guidance and integrated supportive care.

Symptom Management and Perceived Effectiveness

Participants reported a substantial burden of menopausal symptoms, with the most severe symptoms including low sex drive, insomnia, and vaginal dryness, alongside moderate fatigue, cognitive complaints, and hot flashes. Supplements were primarily used for symptom relief, bone health, and general wellbeing, with herbal products more commonly used for cognitive or menopausal symptom management.

Perceived effectiveness of supplements was moderate, with approximately 15% to 25% of reported supplements perceived as ineffective for the symptoms they were intended to address. This variability warrants further investigation. Importantly, large cohort studies and meta-analyses have not demonstrated clear benefits of dietary or herbal supplements in alleviating symptoms or improving overall survival among cancer patients and survivors (7,35).

These findings are particularly relevant given evidence suggesting that many cancer survivors underestimate the risks associated with self-medication. Maraud et al. (2023) reported that 84.9% of cancer patients and survivors believed that self-medication, including the use of dietary and herbal supplements, could not lead to drug interactions

with anticancer treatments, and 84.6% believed that it could not lead to adverse effects (10). These findings reiterate the need for structured clinical education for cancer survivors. In the present study, qualitative data provide insight into why supplement use persists despite limited evidence of efficacy, particularly in contexts where conventional treatment options for menopausal symptoms are contraindicated or perceived as inadequate. Together, these findings highlight the need for patient-centred, symptom-specific, and individualised supportive care for iatrogenic menopausal symptoms.

Source of Information

The internet and social media were the primary sources of information for herbal supplements, whereas clinicians were more commonly consulted for vitamin and minerals. Registered dietitians were rarely consulted (<3%), revealing a critical gap in multidisciplinary survivorship care. Qualitative themes of self-directed research and reliance on peers or online sources reflect patient empowerment but also raise concerns about misinformation. This reliance on online and peer-based information sources aligns with Irish data reported by Keaver et al. (2021), where 74% of breast cancer survivors cited the internet as their primary source of nutrition information and 40.3% cited social media (36). Similar patterns have been reported internationally, including by Kristoffersen et al. (2024) who found that 89.4% of cancer survivors gathered/received information around dietary supplements, with 34% having used social media (12).

While online resources can support patient empowerment, they also pose risks of misinformation. Social media content related to supplements often lacks safety warnings, exaggerates efficacy, and may include financial incentives (37–39).

Although some cancer centre and charity websites score moderately to highly on reliability using tools such as DISCERN (39), reliance on peers, family members, and other survivors remains common, consistent with findings from Malaysian (32) and US cohorts (20). The minimal involvement of dietitians highlights an underutilised opportunity for evidence-based guidance within survivorship care.

Disclosure of Supplement Use

Only around half of participants disclosed supplement use to their healthcare providers, consistent with existing survivorship research indicating under-reporting of complementary medicine use. These finding highlights the systemic barriers that supportive survivorship care face. Previous studies have reported non-disclosure rates ranging from 21.6% to 46.1%, often because clinicians did not ask or patients perceived disclosure as unnecessary (9,10,13,17,18). In contrast, some US and European studies have reported higher supplement disclosure rates of between 51.1% and 82.4% (12,19,20), highlighting variability across healthcare settings and populations.

Qualitative findings from the present study help contextualise these patterns. Disclosure was driven by safety concerns and trust in clinicians, whereas non-disclosure was influenced systemic barriers such as time constraints, perceived disinterest, and fragmented follow-up care. Systemic barriers, including an acute care focus and limited survivorship consultations, may further hinder open communication. Notably, Silver, Goldenberg and Moore (2022) reported that none of their US breast cancer cohort had supplements accurately documented in medical records (40), underscoring the limitations of relying solely on clinical documentation.

Frameworks proposed by Frenkel, Morse and Narayanan (2023) emphasise the importance of routine, non-judgmental inquiry about supplement use within survivorship care pathways (41). Such approaches may enhance patient safety, optimise symptom management, and strengthen clinician-patient trust.

Implications for Practice and Guideline Gaps

The findings of this study highlight important gaps in survivorship care, particularly regarding the management of iatrogenic menopausal symptoms. While non-hormonal pharmacological approaches are increasingly discussed in guidelines, such as those outlined in *The Lancet's 2025 "Menopause Series"* (3), dietary and lifestyle strategies remain under-emphasised in practical guidance for multidisciplinary teams. This may reflect limited awareness of dietetic roles, underfunding of dietetic services within survivorship care, and a lack of adequately powered trials evaluating dietary and supplement-based interventions.

The high prevalence of self-directed supplement use observed in this study suggests that survivors are actively seeking solutions to unmet symptom management needs. Integrating structured, evidence-based dietary and supplement guidance into survivorship pathways may help address these gaps, reduce reliance on potentially unsafe information sources, and support informed decision-making.

Limitations

Several limitations should be acknowledged. The sample was small, highly educated and digitally literature, limiting generalisability to underserved and cancer populations as well as cancer survivors impacted by iatrogenic menopause. The predominance of breast cancer survivors also restricts applicability to other cancer types, although the

findings provide a foundation for broader research. The cross-sectional nature of the study cannot determine whether symptoms preceded supplement use, if severity influenced the commencement of supplements or if supplement use changed over time. Self-reported data, including symptoms, exposures and outcomes may introduce recall and social desirability bias, particularly regarding supplement effectiveness and disclosure behaviours. Future research should aim to clinically validate these factors to ensure clinical relevance and applicability. A key strength of this study is the inclusion of open-text responses, which provided nuanced insights into motivations for supplement use and disclosure behaviours.

Implications for Future Research

Future research should prioritise: (i) rigorous efficacy and safety trials for commonly used herbal and vitamin or mineral supplements in cancer survivors; (ii) interventions to improve patient–clinician communication and routine disclosure in clinical practice; (iii) development of evidence-based educational resources or survivorship toolkits tailored to iatrogenic menopausal symptom management; and (iv) exploration of psychological and behavioural drivers underlying self-directed supplement use.

6.7 CONCLUSION

Poly-supplement use for iatrogenic menopausal symptom relief was highly prevalent among cancer survivors in this small sample, with reported symptoms, motivations for use and patterns of supplement selection being highly individualised. Participants most commonly cited the internet and social media as sources of information, highlight the prominence of non-clinical information channels in shaping supplement use. Disclosure of supplements use to healthcare professionals varied and appeared

to be influenced by both system-level and relational factors, with qualitative findings identifying key perceived motivators and barriers. While limited by sample size, these findings provide descriptive insight into current patterns of supplement use in this population and underscore the need for further large-scale research to better characterise prevalence, information sources and disclosure practices in cancer survivorship.

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CHAPTER 7: MENOPAUSE, DIET AND CANCER: INNOVATING NUTRITIONAL SUPPORT FOR CANCER SURVIVORS IMPACTED BY IATROGENIC MENOPAUSE THROUGH A MULTI-MODAL APPROACH

This work has been streamed by the Irish Cancer Society in September 2024 https://tinyurl.com/menodietcancer and published by CityPrint Ireland © in May 2025 with support from the Irish Cancer Society:

Johnston, K. E., & Cushen, S. J. (2025). Menopause, diet & cancer: Eating well after cancer. School of Food and Nutritional Sciences, University College Cork. https://www.cancer.ie/menopauseplate

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7.1 ABSTRACT

Introduction: Cancer survivors experiencing treatment-induced (iatrogenic) menopause face significant and often unmet nutritional, metabolic, and behavioural challenges. Despite these risks, existing dietary guidelines are broad and generic, offering limited practical guidance tailored to this high-risk population. Survivors report a strong need for credible, actionable dietary advice but frequently encounter barriers to accessing appropriate resources, alongside heightened vulnerability to disordered eating and misinformation. *Menopause, Diet and Cancer* addresses this gap by developing and evaluating the first evidence-based dietary framework and multi-modal educational resources specifically designed for cancer survivors experiencing iatrogenic menopause.

Methods: A co-designed approach was employed. A multidisciplinary review panel (n = 15) including healthcare professionals, academics, and patient advocates guided resource development. Virtual focus groups with sixteen survivors informed symptom-specific priorities, barriers, and preferences. A Mediterranean-style dietary model, *The Menopause Plate* ©, was adapted to the Irish context, emphasising key nutrients relevant to iatrogenic menopause. Thirty-two recipes were developed and nutritionally analysed, incorporating practical considerations such as preparation time, family suitability, and flexibility. Educational resources included a patient-centred book, symptom-specific menus, and a five-part webinar series.

Results: *The Menopause Plate* © and associated recipes met recommended intakes for fibre, calcium, and energy while aligning with Mediterranean dietary principles. The multimodal resources reached over 12,500 engagements across webinars, book distribution, downloads, and online PDFs. The most accessed webinar addressed body

composition and bone health. In 2025, over 2,700 books were distributed throughout Ireland, with 3,331 downloads and 3,934 views of an online PDF version. The webinar series received 233 live registrants, a 329% increase on the Irish Cancer Society's previous two-year average. There were 2,248 individual views and 463 entire series views on the webinar series. The co-design process ensured alignment with survivor priorities and needs.

Conclusion: *Menopause, Diet and Cancer* successfully developed and disseminated the first comprehensive, evidence-based dietary resources specifically for cancer survivors experiencing iatrogenic menopause in Ireland. By prioritising reach, accessibility, and equity of access, this initiative increased engagement across multiple formats and provided an actionable model for delivering tailored dietetic support to an underserved population. These findings highlight the feasibility and acceptability of co-designed nutrition education within survivorship care and lay the groundwork for future evaluation of behavioural and clinical outcomes.

7.2 INTRODUCTION

Despite the growing recognition of the importance of lifestyle and nutrition in survivorship, current dietary guidelines for cancer survivors remain generic, fragmented, and lacking in specificity for high-need groups such as women with hormone receptor-positive breast cancer, gynaecologic cancers, or those experiencing iatrogenic menopause. This gap in specificity highlights a broader problem in survivorship care, wherein the needs for nuanced and tailored information is increasingly evident. In a 2020 scoping review investigating the needs, preferences and experiences of adult cancer survivors (n = 49% breast cancer), needs for accessing dietary information post-treatment included healthy eating behaviours, strategies to manage side effects, complementary alternative medicine safety and efficacy and support in changing dietary behaviours (1). These reported needs align with emerging evidence suggested that survivors require more than generic advice; they require structured, evidence-informed guidance (2).

Survivors highlighted that they preferred specific recommendations, dietary information for overall health and wellbeing beyond treatment recovery, autonomy and self-management but that they had difficulty identifying credible information sources and had limited dietary follow-up (1). This difficulty in accessing credible information underscores the shortcomings of current survivorship care pathways. Furthermore, young breast cancer survivors have reported several unmet needs, including those around nutrition and iatrogenic menopause (3). A 2025 qualitative study identified that Irish women experiencing an iatrogenic menopause following breast cancer treatment received little or no meaningful support from healthcare professionals despite available opportunities for healthcare education (4). Collectively, these unmet needs highlight a systemic disconnect between what cancer

survivors require and what is currently provided within survivorship care. To understand the roots of this disconnect, it is essential to examine the nutritional guidance frameworks that shape clinical practice and consider their limitations.

Looking to the current nutritional guidelines available, the European Society of Clinical Nutrition and Metabolism (ESPEN) and European Society of Medical Oncology (ESMO) guidelines provide only broad recommendations around healthy weight, physical activity, and plant-based diets, based on low-level evidence and without tumour-specific nuances (5,6). While these guidelines offer a foundation they do not adequately address the complex needs of women experiencing iatrogenic menopause. The American Cancer Society guideline goes further by linking obesity, diet, and physical activity with outcomes in breast cancer, yet still falls short of offering concrete, individualised dietary strategies (7). Similarly, despite adopting a more multidisciplinary orientation, the National Cancer Comprehensive Network (NCCN) survivorship guidelines incorporate body composition assessment but again focus on broad "healthy eating" principles rather than addressing the unique metabolic and endocrine challenges faced by these populations (8).

However, beyond the limitations of existing guidelines, behavioural and psychological factors add complexity to eating during and after iatrogenic menopause. This cohort may be particularly vulnerable to disordered eating and weight-related concerns (9–12), highlighting the important of dietary interventions that are sensitive to not only metabolic needs, but also to the psychosocial context. These considerations underscore the need for carefully structured, evidence-informed nutritional education, Nucci et al. (2022) emphasised the importance of appropriate dietary counselling and nutritional evaluation particularly in the context of misinformation and misinterpretation of dietary advice on the internet (10). Whilst Loeliger et al. (2024) highlights that in the

absence of dietetic resources and lack of access, co-designed nutrition resources are highly acceptable to both service users and healthcare professionals (13).

Given the convergence of guideline gaps, survivor-reported needs, and behavioural health risks, bridging these requires a comprehensive, integrative response. Cancer survivors have consistently highlighted their desire for specific nutrition education through a variety of modalities delivered by registered dietitians during the survivorship care continuum (2,14,15), yet resources remain few and far between.

Existing evidence highlights a persistent gap between the dietary needs of women experiencing iatrogenic menopause and the guidance currently available. To date, no evidence-based dietary model or patient-facing resource specifically addresses the nutritional needs of cancer survivors in this context. Building on earlier chapters that identified unmet nutritional needs in survivorship care, this chapter presents the co-design and dissemination of tailored dietary resources for this population, translating identified needs into practical, evidence-informed interventions that aim to improve reach, engagement, and equitable access.

7.3 AIMS

The aim of this research is to develop and deliver practical, evidence-based nutrition advice tailored to this population. The objectives are (1) support the management of menopause-related symptoms (e.g., hot flushes, weight gain, bone loss), (2) reduce long-term health risks associated with cancer treatment, (3) address common nutrition misconceptions, and (4) enhance engagement and access to nutritional support through a multimodal educational approach integrating recipe development, a patient-focused book, and a webinar series.

7.4 METHODS

7.4.1 Conceptualisation and Project Timelines

Results from a previously published study conducted by our research group in University College Cork revealed female cancer survivors experience a substantial burden from iatrogenic menopausal symptoms and feel lost due to unmet needs for accessible, evidence-based, and tailored nutrition information to help them regain control and manage symptoms during survivorship (16). These discussions provided essential insights into women's needs, concerns, and preferences. Building on this, in 2022 the LYSA team and stakeholders discussed developing a nutrition booklet specifically for cancer survivors experiencing iatrogenic menopause, following use of the "Healthy Eating for Cancer Survivors" resource (17) in the Irish Cancer Society's Women's Health Initiative LYSA Trial (18). In early 2024, the Irish Cancer Society requested a webinar series on Menopause, Diet and Cancer, and it was agreed that a symptom-specific webinar series would be developed to provide timely access to dietary guidance while the book was in production. The project was conducted between September 2022 and December 2025. A comprehensive timeline of the project can be found in Figure 7.1.

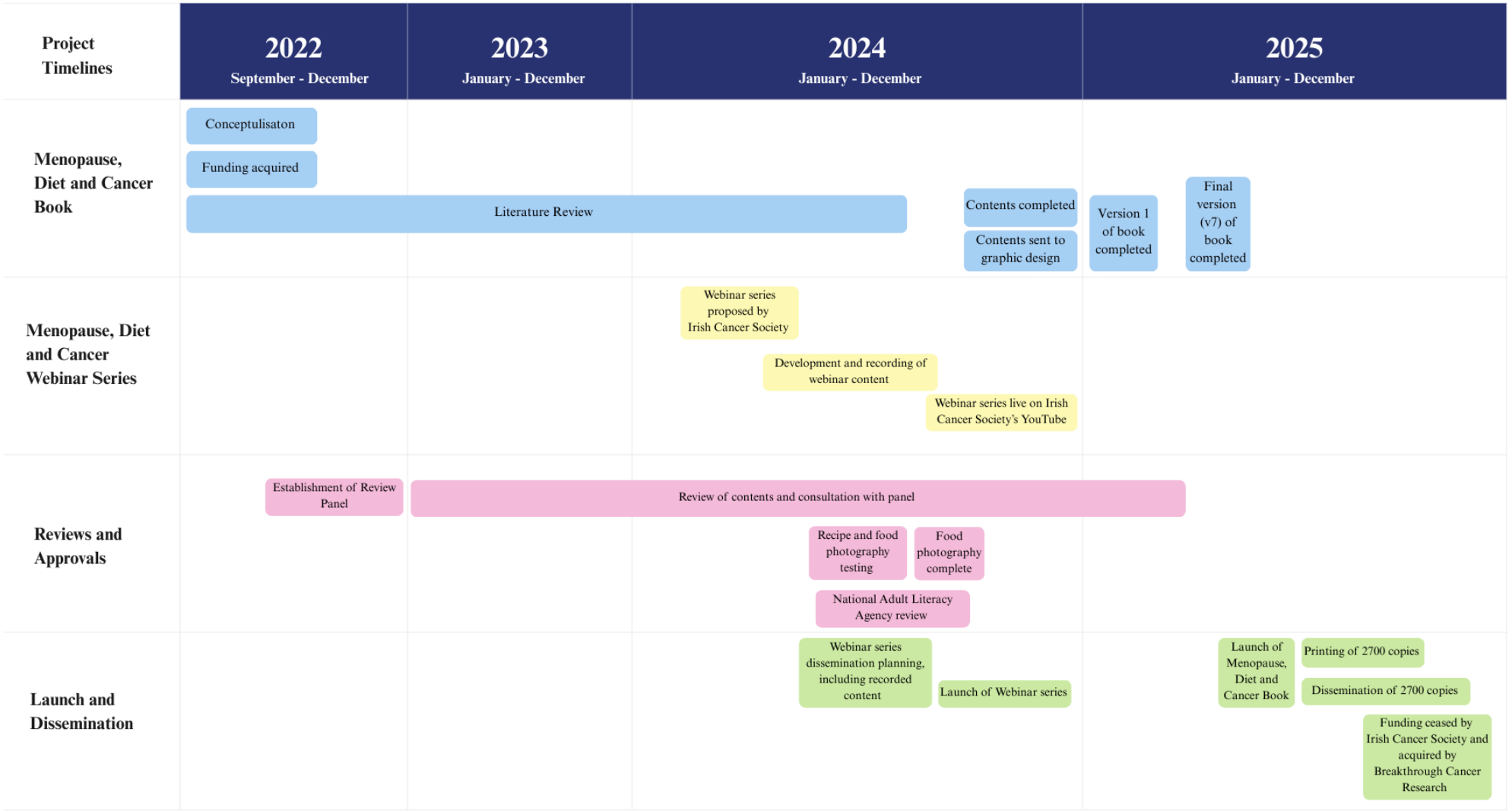


Figure 7.1: Menopause, Diet and Cancer Project Timeline

7.4.2 Establishing an interest group and review panel

A review panel was established in October 2022 to provide iterative input on the development of the Menopause, Diet and Cancer resources. The panel comprised fifteen members from diverse clinical, academic, advocacy, and patient support backgrounds, including a medical oncologist (n = 1), clinical nurse specialists (n = 2), professors in nutrition and nursing (n = 2), a pharmacist (n = 1), dietitians (n = 3), academics (n = 1), a psycho-oncologist (n = 1), a patient advocate (n = 1), representatives from the LGBTQIA+ community (n = 2), and representatives from the Irish Cancer Society (n = 2).

The role of the panel was consultative and advisory rather than formal co-design. Members were engaged at key stages of the project and provided feedback relevant to their expertise, including clinical accuracy, patient acceptability, and clarity of educational content. Materials were circulated to relevant members for review as each component was developed, and feedback was incorporated iteratively by the research team.

In addition, the project was discussed within steering committee meetings of the Irish Cancer Society Women's Health Initiative, providing broader stakeholder input. Patient and public involvement (PPI) insights informing the project were primarily drawn from previously published qualitative work conducted by the research team in this population, which explored lived experiences of iatrogenic menopause following cancer treatment (16). These findings informed the initial prioritisation of topics and shaped the structure of the resource.

Funding support was provided by the Irish Cancer Society Women's Health Initiative and a private donation.

7.4.3 Literature Review

From September 2022 to July 2024 a comprehensive literature review was undertaken, elements of which are presented in Chapter 1 of this thesis. A brief overview of the search strategy is provided in Table 7.1 Databases used in the search included PubMed, Web of Science, Google Scholar and PyschINFO. Furthermore, a thorough literature review was conducted including position statements (19), clinical guidelines, patient-facing websites, such as Memorial Sloan Kettering, clinical cancer nutrition guidelines and cancer societies (Table 7.1). The literature review was then devised to symptom-specific outcomes that were evaluated through the LYSA Trial (18,20), including body composition (musculoskeletal; adiposity; and bone composition); cardiovascular; vasomotor; genitourinary and gastrointestinal; and cognitive function. A separate literature review was conducted investigating symptom-specific supplements, efficacy and safety. The review focused on collecting evidence from international nutrition guidelines, meta-analysis and systematic reviews and randomised controlled trials first, before exploring evidence from observational and cohort studies (21). The National Adult Literacy Agency (NALA) was consulted at the point of refinement and sent a sample of the content. The literature was refined based on the advice from NALA and the review panel.

Table 7.1: A Brief Overview of *Menopause, Diet and Cancer* Literature Review Sources

Category	Source
Position Statements	European Menopause and Andropause Society (19)
Clinical Guidelines	American Cancer Society (7) American Society of Clinical Oncology (22) European Society of Medical Oncology (6) Clinical Oncology Society of Australia National Cancer Control Programme (23) World Cancer Research Fund (24)
Websites	Memorial Sloan Kettering Cancer Centre ThisisGO.ie
Clinical Cancer Nutrition Guidelines	European Society of Clinical Nutrition and Metabolism (5) American Society of Clinical Nutrition and Metabolism
Cancer Societies	Irish Cancer Society Marie Keating Foundation Macmillan
Scientific Literature	PubMed Web of Science Embase Google Scholar PychINFO

7.4.4 Devising a Dietary Model

A targeted review of international dietary guidelines was conducted to inform the dietary model. Priority was given to dietary guidelines aligned with a Mediterranean-style eating pattern and principles as supported by position statements from the European Menopause and Andropause Society (19). This evidence-base was adopted as the foundation for *Menopause, Diet and Cancer*. To determine the most effective format for communicating this dietary advice a review of existing national food-based dietary guidelines was undertaken including the Healthy Ireland's Food Pyramid (25); the United Kingdom's Eatwell Guide (26); the Canadian Food Guide Plate (27); and the Austrian "*Der gesunde und nachhaltige Teller*" (Healthy and Sustainable Plate) Model (28). Based on this review, the Canadian and Austrian plate models were identified as the most suitable presentation formats for the *Menopause, Diet and Cancer* target population. These approaches were considered both visually impactful

and conceptually inclusive, avoiding the hierarchical implications of the food pyramid and the dichotomy of “good” versus “bad” foods. Accordingly, a menopause- and cancer-specific dietary plate model was developed grounded in Mediterranean dietary principles and contextualised for the Irish population.

Initial selection criteria of recipes included alignment with Mediterranean dietary principles, accessibility of ingredients, preparation time, and family suitability Recipes were adapted from previously published recipes with permission from the authors or developed by authors themselves. Each recipe was evaluated using sensory science principles for taste, feasibility, visual appeal, and nutritional balance (29). Oral and written feedback informed iterative refinements to enhance variety, practicality, and adherence to Mediterranean principles. Recipes not meeting these criteria were excluded in the final collection.

Nutritional composition was assessed using Nutritics (Nutritics Ltd., Dublin, Ireland). Following guidance from the European Commission (30) and the Food Safety Authority of Ireland (31) analysis was based on per 100g and per portion and adjusted for cooking yield where relevant. Macro- and micro-nutrient profiles were generated for each recipe following guidance from the Food Safety Authority of Ireland (32), with a focus on nutrients of relevance to individuals affected by iatrogenic menopause, including those associated with bone health, cardiovascular function, and muscle mass. Nutritional requirements were calculated using a reference profile of a 55-year-old female, reflecting the median age of participants in The LYSA Trial. This approach ensured that energy and nutrient estimates were representative of the typical physiological and metabolic characteristics of the intended population, while remaining practical and broadly applicable. Given evidence from prior research by

Sullivan et al. (2021) (15) that cancer survivors are often overwhelmed by conflicting nutritional information, a simplified approach to nutrient labelling was adopted. Nutrient labels highlighted only the key components discussed throughout the educational resource: energy, protein, fibre, saturated fats, salt, and calcium. Nutritional labels were presented by serving size (32). Allergens were presented below the label (30,32).

A nutritional key (Table 7.2) was developed to present these elements in an accessible, reader-friendly format, presented at the top of the recipe as icons. The guidelines followed the European Commission's *Nutrition and Health Claims* (Regulation (EC No 1924/2006) for Saturated Fat, High Fibre, Low Sodium, Source of Protein, and a Source of Calcium (30). In addition to the nutrient key, symptom-orientated ingredient mapping was developed for each recipe, mapping specific ingredients to common symptoms associated with iatrogenic menopause. This label was informed by findings from the literature review and aimed to connect the two educational components of the book, *information giving* (nutritional education) and *information implementation* (practical application in recipes), using the principles of the Experiential Learning Framework by Kolb (1984) (33). For example, ingredients such as oats or calcium-rich dairy products were linked to evidence-based benefits related to gut health and bone health. This approach was designed to promote active learning, helping readers understand why particular ingredients were chosen and how they relate to managing menopause-related symptoms, thereby reinforcing dietary adherence and self-efficacy.

Table 7.2: Menopause, Diet and Cancer Recipe Key

Recipe Key	Explanation
High in Protein	More than 20% of total energy from protein
High in Fibre	More than 6g of fibre per 100g of food
Source of Calcium	More than 120mg of calcium per 100g of food
Heart Healthy	Less than 1.5g of saturated fat and 0.5g of salt per 100g of food
Timesaver	Recipe is ready in under 30 minutes
Meat-Free Option	Vegetarian friendly recipe

Source: European Commission's *Nutrition and Health Claims* (Regulation (EC No 1924/2006) (30).

Final recipe testing was completed in July 2024. A subset of recipes was prepared and photographed to inform collaboration with the food photographer and stylist (Figure 7.2). A vision board was subsequently developed for each recipe (Figure 7.3) to guide presentation style and maintain consistency across the collection. Presentation and photography decisions were informed by health literacy principles (34,35) and feedback aiming to emphasise the colourful, appetising, and family-friendly aspects of the Mediterranean style of eating. Visual design also reflected the importance of accessibility and engagement for individuals recovering from cancer treatment, supporting positive food identity and confidence in dietary self-management (34). Finalised food photography was completed in August 2024.



Figure 7.2: Recipe Testing and Food Photography Test of *Menopause, Diet and Cancer* Recipes Conducted in July 2024

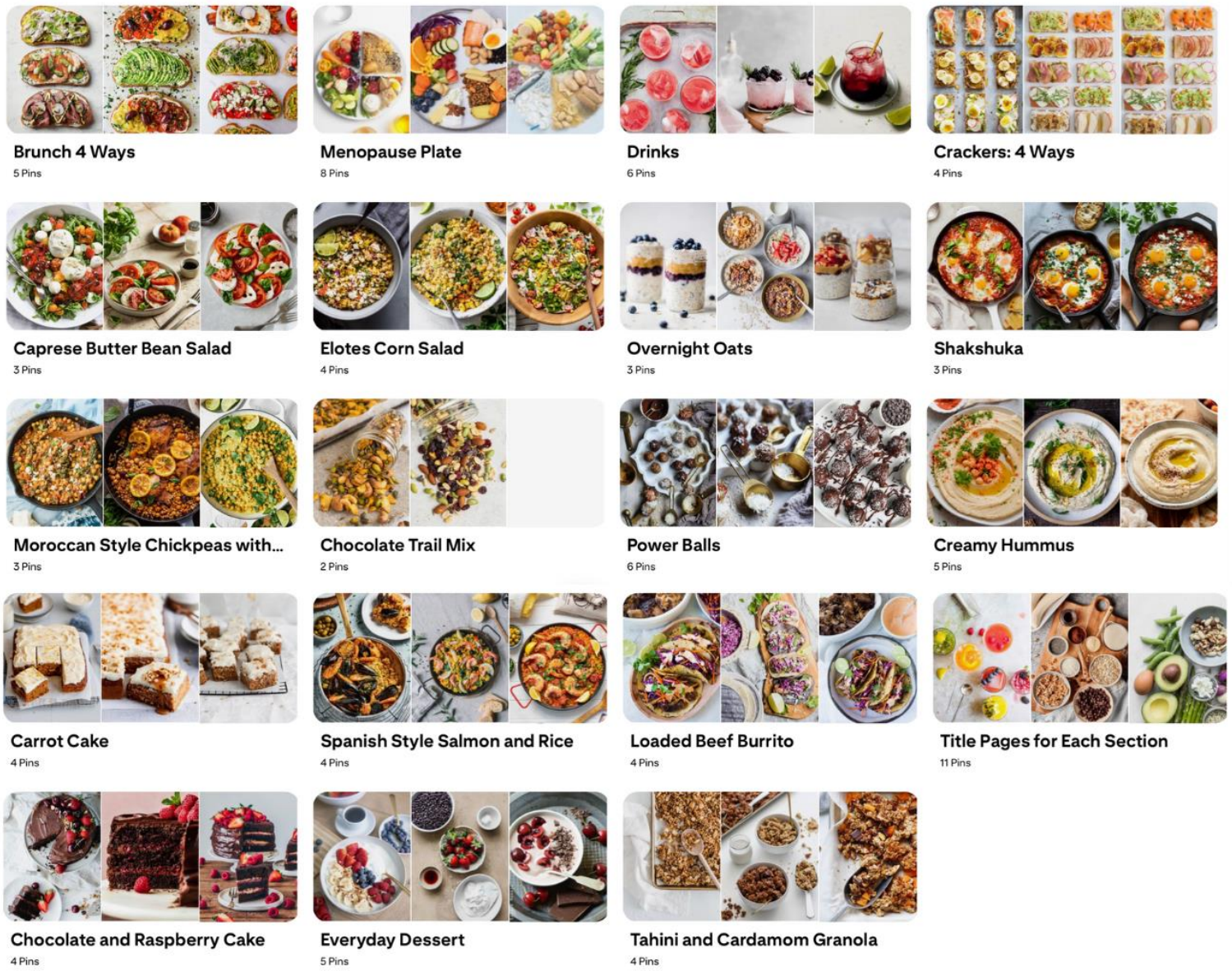


Figure 7.3: Vision Board for Styling and Photography of *Menopause, Diet and Cancer* Recipes

7.4.5 Design of the Book

The final educational resource was developed through an iterative, multi-stage process involving the research team, a graphic designer, and the multidisciplinary review panel described above. While the development process was informed by principles of patient-centred design (36), it did not follow a formal co-design framework such as Experience-Based Co-Design (EBCD). Instead, patient and stakeholder input was integrated through structured feedback cycles and targeted consultation.

Input from patient representatives, drawn from prior qualitative research within the programme of work, informed the structure, content priorities, and tone of the resource. Expert stakeholders contributed feedback on clinical accuracy, safety, and appropriateness of dietary recommendations.

Following initial compilation, the resource underwent repeated review cycles. Feedback was used to refine clarity, usability, inclusivity, and accessibility. This included the addition of symptom-focused sections, practical implementation guidance, and patient-informed FAQs to reflect common concerns identified in both prior research and stakeholder consultation.

A QR code linking to an anonymous feedback form (Qualtrics) was included in the final publication to support ongoing user feedback and iterative refinement of future editions.

7.4.6 Statistical Analysis

Quantitative data were analysed using R Software Package (37) and Microsoft Excel (Microsoft Corp., Redmond, WA, USA). Descriptive statistics were used to

summarise the nutritional composition of individual recipes and recipe categories, and to characterise engagement metrics from the webinar series and book dissemination. Results are presented as means ± standard deviations (SD) for continuous variables and as frequencies and percentages for categorical variables. The nutritional analysis was conducted using the nutrient composition data generated by Nutritics (Nutritics Ltd., Dublin, Ireland). Mean energy and nutrient content (per 100g and per portion) were calculated for each recipe and aggregated by recipe category (breakfasts, light meals, main meals, snacks, desserts, and drinks). Deviations from reference values were described narratively, with no inferential statistical testing applied given the descriptive, exploratory nature of the dataset. Engagement metrics were prospectively collected from platform analytics (e.g. YouTube Studio, Irish Cancer Society reporting dashboards, website analytics) and extracted for descriptive analysis. For webinar engagement data, view counts, registrations, and participation metrics (e.g., number of live attendees, submitted questions) were analysed descriptively. Trends in viewership and engagement across webinars were presented as frequencies and relative percentages. Data presentation aimed to provide a comprehensive overview of the nutritional profile of the recipes and engagement with the educational resources inform future iterations of the *Menopause, Diet and Cancer* programme.

7.5 RESULTS

7.5.1 Development of a Dietary Model

The *Menopause Plate* © (Figure 7.4) was developed using the Mediterranean Diet principles adapted for an Irish diet, and the nutritional considerations identified through the literature review for those affected by iatrogenic menopause, such as the

inclusion of soya isoflavones, calcium, and plant stanols and sterols. Following the plate-model The *Menopause Plate* © is comprised of 50% fruit and vegetable sources, 25% of wholegrain carbohydrate sources and 25% of protein sources, with a mix of animal and plant-based origins, excluding processed meat as per the World Cancer Research Fund Guidelines (24).



Figure: 7.4: The *Menopause Plate* ©

7.5.2 Nutritional Composition of Meals

A total of 32 recipes were developed for *Menopause, Diet and Cancer*. These comprised five breakfast recipes, six light meals, three main meals, eight snacks, six desserts, and four drinks. The nutritional composition of individual recipes is detailed in Table 7.3 while the mean nutritional composition for each recipe category is presented in Table 7.4.

The mean protein content was 20.4g ± 8.7g for breakfasts, 25.3g ± 7.6g for light meals, 36.7g ± 15.8g for main meals, 12.0g ± 4.9g for desserts, and 7.2g ± 3.1g for snacks. The mean fibre content was 8.4g ± 3.7g for breakfasts, 9.8g ± 6.7g for light meals, 12.6g ± 5.1g for main meals, 4.2g ± 1.1g for snacks, and 2.8g ± 0.8g for desserts. Of the total recipes, seventeen were classified as high in protein, thirteen as high in fibre, thirteen as a source of calcium, eighteen as heart healthy, twenty-six as ready within thirty minutes or less, and twenty-six as meat-free options.

Using the mean nutritional composition from the recipe categories to model a daily meal plan consisting of three meals and two snacks for a 55 year old female, the mean energy content aligned with EFSA recommendations for daily energy intake across varying physical activity levels (1783kcal to 2547 kcal) (38). The modelled plan exceeded the EFSA recommended intake for fibre (25g/day) (39) and calcium (950mg/day) (40), while meeting the sodium recommendation (2g/day) (41).

Table 7.3: Nutritional Analysis of Recipes included in *Menopause, Diet and Cancer*

Recipe (values per serving)	Serving Size	Energy (kcal)	Fat (g)	Sat fat (g)	Fibre (g)	Protein (g)	Salt (g)	Calcium (mg)
Breakfast								
Tahini and Cardamom Granola	40g	204	14	1.9	3.1	5.1	0	54.4
Shakshuka: Family Style	549g	338	17	5.5	7	22	0.89	183.92
Overnight Oats								
Tropical	402g	396	8.4	1.9	8.9	25	0.35	385.92
Raspberry and Dark Chocolate	362g	397	11	3.7	13	26	0.33	369.24
Nut Butter and Wild Blueberries	288g	427	17	2.9	9.8	24	0.25	302.4
Light Meals								
Brunch 4 Ways								
New York Style	218g	345	11	3	3.8	30	1.6	207.1
Korean Style	150g	416	23	3.4	7.3	17	0.74	75
Melbourne Style	255g	515	32	7.3	5.3	25	0.63	165.75
Mexican Style	266g	343	9.4	3.1	13	16	0.62	122.36
Elotes Corn Salad with Chicken	466g	379	14	3.7	7.6	35	0.31	70.83
Caprese Butter Bean Salad	480g	404	13	5.6	22	29	0.4	345.6
Main Meals								
Moroccan Chickpea Stew with Crispy Tofu	514g	366	12	1.6	12	23	0.41	472.88
Loaded Beef Burrito	556g	737	21	6.9	18	54	2.1	289.12
One Pan Spanish Salmon and Rice	625g	582	19	3.5	7.9	33	1.2	71.25
Snacks								
Creamy Hummus	58g	114	11	1.5	3.2	5.7	0.15	121.22
Chocolate Trail Mix	29.3g	168	13	2.3	2.4	5.2	0.01	28.71
Kate's Kitchen Peanut Butter Balls	43g	185	8.7	1.5	4.6	5.8	0.04	32.25

Recipe (values per serving)	Serving Size	Energy (kcal)	Fat (g)	Sat fat (g)	Fibre (g)	Protein (g)	Salt (g)	Calcium (mg)
Brain Bites	26g	103	4.8	1.6	3	3.8	0.02	34.3
Crackers: 4 Ways	22g	81	1.6	0.3	4	2.5	0.13	19.58
New York Style	107g	136	4.1	1.8	4.5	7.4	0.7	177.62
Italian Style	128g	153	5	2.6	4.8	8.9	0.31	134.4
Moroccan Style	59g	195	10	1.6	5.7	6.9	0.21	112
English Style	146g	312	17	9.9	5	14	0.93	348.94
Desserts								
Carrot Cake with Tahini Cream Cheese	102g	368	21	4	1.9	7.8	1	172.38
Chocolate and Raspberry Traybake	93g	197	5.9	1.9	3.5	4.1	0.27	59.52
The Everyday Dessert								
Summer Berry	216g	117	0.5	0	2.9	14	0.21	183.6
Apple Crisp	200g	199	7	1	2.4	16	0.21	198
Peaches and Cream	206g	141	3.4	0.3	2.1	15	0.21	189.52
Chocolate and Strawberries	208g	179	6.2	3.6	4	15	0.2	191.36
Drinks								
Cooling Mint and Ginger Iced Tea	310mls	27	0	0	0.5	0.5	0	3.72
Nu-Go Spritz	174mls	39	0.6	0.1	0.5	0.8	0.03	8.87
Refreshing Blueberry No-jitos	190mls	34	0	0	0.5	0.5	0.08	11.02
Spiced Cherry Fizz	145mls	105	0	0	0.6	1.3	0.02	23.49

Abbreviations: g, grams; kcal, kilocalories; mg, micrograms

The recipe collection was designed to prioritise practicality, flexibility, and accessibility (Figure 7.5). Recipes were suitable for advance preparation or could be prepared in under thirty minutes, making them appropriate for family use and varying time constraints. Breakfast, light meal and snack recipes were developed from common foundational bases that allowed for variation in flavour and ingredients, and several recipes could be adapted for on-the-go consumption. The collection incorporated both hot and cold options, as well as non-alcoholic beverages. The inclusion of desserts emphasised the importance of dietary variety and balance while promoting a neutral and inclusive perspective on food choices.

Looking at adherence to selected principles of the Mediterranean Diet, each recipe met at least one principle. The collection of breakfast recipes met two to four principles per serving, light meals met three to five principles, and main meals also met three to five principles, reflecting their higher content of vegetables, legumes, wholegrains, and moderate protein sources. In contrast, snacks met one to three principles, and desserts met one to two principles, contributing mainly through fruit, nuts, or dairy rather than wholegrains or protein (Supplementary Table 7.1). Some recipes, for example Tahini and Cardamom Granola and Creamy Hummus, were developed as a base allowing readers to add their own elements, such as fruit and vegetables, a protein or dairy source, using the principles from The *Menopause Plate* ©.

Table 7.4: Mean Nutritional Composition of Recipe Collections

Recipe Collection	Energy (kcal)		Fat (g)		Saturated Fat (g)		Fibre (g)		Protein (g)		Salt (g)		Calcium (mg)	
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
Breakfast	352.4	89.0	13.5	3.8	3.2	1.5	8.4	3.7	20.4	8.7	0.4	0.3	259.2	139.3
Light Meals	400.3	63.6	17.1	8.7	4.4	1.7	9.8	6.7	25.3	7.6	0.7	0.5	164.4	103.1
Main Meals	561.7	186.3	17.3	4.7	4	2.7	12.6	5.1	36.7	15.8	1.2	0.8	277.8	201.1
Snacks	170.8	65.6	9.2	4.5	2.9	2.9	4.2	1.1	7.2	3.1	0.3	0.3	123.7	106.4
Dessert	200.2	88.4	7.3	7.1	1.8	1.7	2.8	0.8	12.0	4.9	0.4	0.3	165.7	52.7
Drinks	51.3	36.2	0.2	0.3	0.0	0.1	0.5	0.1	0.8	0.4	0.0	0.0	11.8	8.4
Mean Total	*1736.6*		*64.6*		*16.2*		*38.3*		*102.4*		*3.0*		*1002.6*	

Abbreviations: g, grams; kcal, kilocalories; mg, micrograms; SD, standard deviation



Figure 7.5: Recipes from *Menopause, Diet and Cancer*

7.5.3 Menopause, Diet and Cancer Book and Webinar Series

The *Menopause, Diet and Cancer* book contains 162 pages of evidence-based information and recipes. It has been endorsed by the Irish Nutrition and Dietetic Institute; the Irish Cancer Society; Breakthrough Cancer Research; and the CUH/UCC Cancer Centre, Cork University Hospital. The authors collaborated with clinical nurse specialists and patient advocates to develop *The Menopause Minefield*, a patient-centred overview of the symptoms and experiences readers may be facing as a result of iatrogenic menopause (Figure 7.6). Each chapter begins with a quote from a woman who has experienced iatrogenic menopause, further embedding the patient voice throughout the resource.

The Menopause, Diet and Cancer webinar series was developed to coincide with Breast & Gynaecologic Cancer Awareness Months and World Menopause Day, allowing for rapid dissemination of dietary guidance while the book was in development [Supplementary Table 7.2]. The webinars mirrored the symptom-focused structure of the book and aimed to enhance understanding and uptake of the resource. Five webinars were created, including a live question-and-answer session, during which 37 questions were submitted, covering topics such as menopause-related symptoms (e.g., vaginal atrophy) and dietary supplements (e.g., tart cherry concentrate), demonstrating active audience engagement.

Feedback from the webinars, including participant questions and engagement trends, was used to refine the content within the book. Seventeen "*Frequently Asked Questions*" were included in the book, derived from practical elements (e.g., reading supplement labels), topical media trends (e.g., seed oils), and questions raised during the live webinar (e.g., use of tart cherry concentrate for arthralgias). Presenting the

webinars prior to the book ensured early engagement with survivors and allowed the written resource to address real, current needs in a practical and responsive manner.

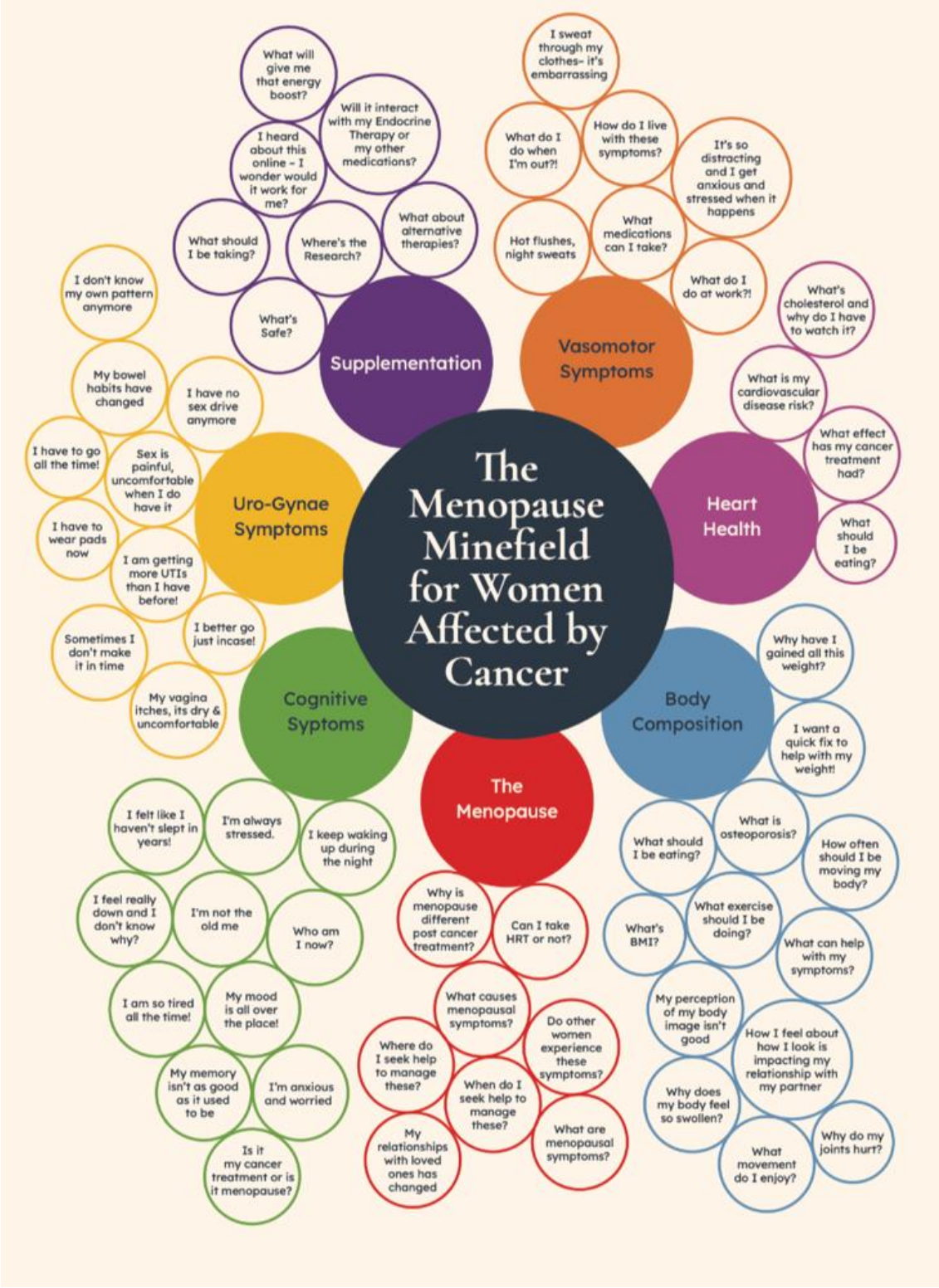


Figure 7.6: The Menopause Minefield for Women Affected by Cancer

7.5.4 Dissemination

The Menopause, Diet and Cancer book (Figure 7.7) was disseminated through a multi-modal strategy led by the Irish Cancer Society, incorporating physical distribution, online access, media engagement, and webinars as a mechanism to support knowledge translation and reach target audiences.

7.5.4.1 Book Dissemination and Access

A press release was issued on the day of the book launch by the Irish Cancer Society communications team and the University College Cork press office, featuring quotes from the authors and a patient representative. An initial print run of two hundred copies was distributed to launch attendees, key stakeholders, and services within regional cancer centres. In June 2025 additional funding supported a second print run of 2,500 copies, which were disseminated to regional cancer centres and cancer support centres nationwide via hand delivery or courier. An online PDF version of the book was made freely available on the Irish Cancer Society website under the Researcher News and Events section, further increasing accessibility.

7.5.4.2 Webinars as a Dissemination Mechanism

In parallel with the book's development, webinars were used as a complementary dissemination mechanism to broaden reach and engagement. The five-part webinar series was delivered between 19 September and 17 October 2024, aligned with Gynaecologic Cancer Awareness Month, Breast Cancer Awareness Month, and World Menopause Day. The webinar series generated three hours and thirty-one minutes of educational content hosted on the Irish Cancer Society's YouTube channel (Figure 7.8). As of 2nd December 2025, the series recorded 2,248 individual video views and 463 full-series views. The most viewed webinar addressed body composition and bone

health (n = 451) while the least viewed focused on gut health and genitourinary symptoms (n = 217).

A total of 233 participants registered for the live webinar, representing a 329% increase compared with the Irish Cancer Society's two-year average webinar attendance and making it their most attended webinar of 2024.

7.5.4.3 Media Reach and Engagement

Promotion of the book and associated webinars across the Irish Cancer Society's social media platforms (Twitter/X, LinkedIn, Facebook, and Instagram) resulted in over 10,000 views of campaign content during the dissemination period. Printed promotional materials distributed to regional cancer centres and cancer support centres supported reach among individuals not actively engaged on social media.

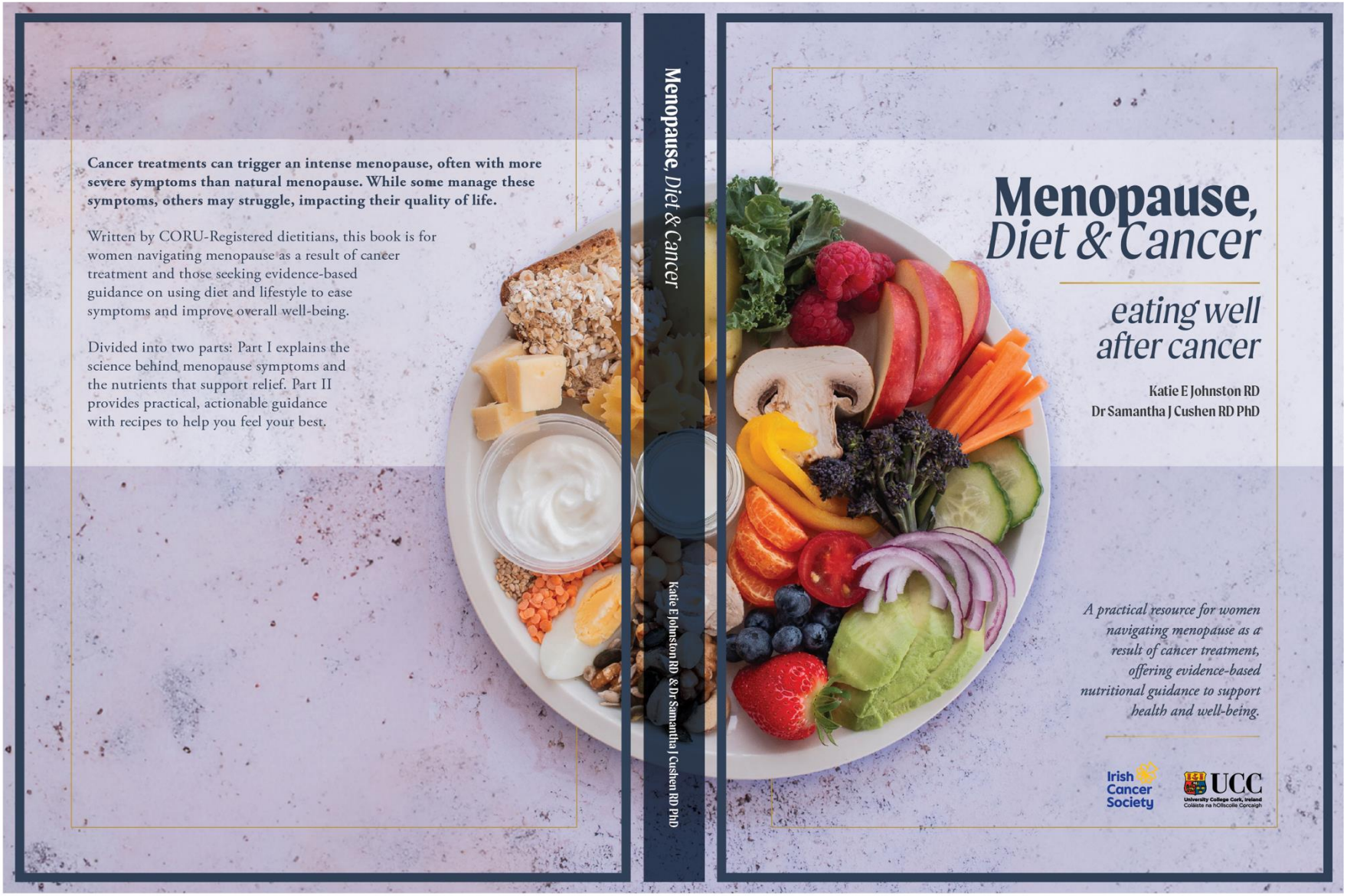


Figure 7.7: Menopause, Diet and Cancer Cover



Figure 7.8: Examples of *Menopause, Diet and Cancer* Webinar Series Content

7.5.6 Launch of Menopause, Diet and Cancer Book

Menopause, Diet and Cancer was officially launched on 28th May 2025 at ARC Cork Cancer Support House (Figure 7.9). A brief programme of speakers was developed for the launch including the authors, the Chief Financial Officer of the Irish Cancer Society, the Programme Manager of Survivorship Research at the Irish Cancer Society, the Assistant Director of Nursing at the National Cancer Control Programme, the Academic Director of CUH/UCC Cancer Centre, Cork University Hospital, Breast Cancer Counsellor from ARC Cork Cancer Support House, and a patient advocate. Approximately sixty healthcare professionals and key stakeholders were in attendance. The number of attendees at the launch was capped due to space capacity and funding available.

In May 2025, *Menopause, Diet and Cancer* books were distributed initially to attendees of the launch, key stakeholders at the Irish Cancer Society, the Women's Health Initiative Survivorship service at Cork University Hospital, the Complex Menopause Clinic at Cork University Maternity Hospital and Cork ARC Cance Support House. Following the allocation of additional funding for printing, 2700 copies were distributed nationwide by the authors throughout Ireland to regional cancer centres, hospitals with designated systemic anti-cancer treatments and cancer support centres. An interactive map was created in July 2025 at the request of the Irish Cancer Society to signpost service users to access the book. As of 2nd December 2025, this map had 2,100 views.

The launch of the book resulted in three newspaper articles, including the Irish Examiner, Irish Daily Mail and Cork Echo, and features in online news bodies including the Medical Independent, Hospital Professional News and the Irish

Pharmacist. Within five weeks of its launch, the online version of the book had 3,054 views and 1,228 downloads on the Irish Cancer Society's website. As of 2nd December 2025, the online version of the book had 3,934 views and 3,331 downloads.

The Irish Cancer Society ceased funding the book in September 2025, and the publication was acquired by Breakthrough Cancer Research in October 2025 with distribution of an initial 6,000 copies expected to restart in early 2026. An online PDF version was agreed to remain on the Irish Cancer Society's website.



Figure 7.9: Launch of *Menopause, Diet and Cancer* in Cork ARC Cancer Support House, Cork, Ireland, on 28th May 2025

7.6 DISCUSSION

This chapter primarily addresses the development, feasibility, and acceptability of a co-designed, symptom-responsive dietary resource for cancer survivors experiencing iatrogenic menopause, rather than evaluating clinical or behavioural efficacy. This project represents the first structured attempt to provide targeted nutrition resources for cancer survivors experiencing iatrogenic menopause, a population whose metabolic, endocrine, and behavioural needs are not adequately addressed in standard survivorship care. The findings underscore the complexity of nutritional support for this cohort, particularly the dual challenge of addressing menopause-related symptom management while mitigating long-term health risks associated with cancer treatment, including musculoskeletal decline, cardiovascular risk, and metabolic dysfunction. The *Menopause Plate* © and associated multimodal resources exemplify a novel, evidence-informed approach to addressing these overlapping health priorities in survivorship care.

The development of a culturally adapted Mediterranean-style dietary model illustrates the feasibility of translating international dietary guidance into a practical and locally relevant framework. By incorporating evidence-based principles for nutrient intake (e.g., protein, fibre, calcium, plant sterols) and aligning meals with symptom-specific outcomes the resources operationalise the theoretical concept of precision nutrition within survivorship. This aligns with contemporary calls in oncology nutrition for personalised dietary interventions that reflect tumour type, treatment exposure, and patient-reported outcomes (e.g., vasomotor, musculoskeletal, or cognitive symptoms). Previous literature has highlighted the beneficial outcomes associated with adherence to a Mediterranean-style of eating across numerous domains including quality of life, cancer and non-cancer related mortality, anthropometric measures, metabolic

outcomes and gut microbiota. Specifically, while large cohort studies have not consistently demonstrated reductions in breast cancer-specific mortality, higher adherence has been associated with significant reductions in overall and non-breast cancer mortality among women with lower physical activity ($p < 0.05$ and $p < 0.001$, respectively), underscoring the potential cardiometabolic benefits in higher-risk groups (42). Intervention studies further demonstrate modest but clinically meaningful improvements in body composition, such as reductions in BMI (-0.87kg/m^2, $p < 0.001$) and waist circumference (-3.93cm, $p < 0.001$) (43); and improvements in glycaemic control such as fasting glucose (-9.1%, $p < 0.001$) and insulin (-18.1%, $p < 0.05$) (44). Evidence for lipid and inflammatory outcomes is more variable, though significant reductions in LDL cholesterol, triglycerides and high-sensitivity C-reactive protein have been reported (45–47). Importantly, several studies have observed improvements in patient-reported outcomes, including global health status, physical and social functioning, and reductions in fatigue (all $p < 0.05$) (47,48). Collectively, these findings support the Mediterranean dietary pattern as a flexible, food-based framework capable of addressing key nutritional, metabolic, and quality-of-life concerns in breast and gynaecologic cancer survivors, providing a strong rationale for its adaptation within the Menopause Plate model. Furthermore, the use of a plate-based visual model facilitates understanding and practical implementation, bridging the gap between abstract nutritional recommendations and actionable behaviours, which is a recognised challenge in nutrition literacy for survivors (49).

The iterative development approach represents a key strength of the project, ensuring that the resources are both scientifically robust and responsive to patient experience and multidisciplinary expertise. Integration of patient voices through focus groups, coupled with feedback from a multidisciplinary review panel aligns with best practice

in patient-centred intervention development. This approach also reflects principles of experiential learning, whereby patients are empowered to understand the rationale for specific dietary choices, reinforcing adherence and self-efficacy. By embedding symptom-specific guidance, FAQs, and "Dietitian's Top Tips," the resource provides scaffolding for behaviour change, acknowledging the cognitive load and conflicting nutritional information that survivors often encounter post-treatment.

Engagement metrics and qualitative feedback highlight the relevance and acceptability of the resources. The high viewership of webinars on body composition and bone health suggests that survivors prioritise guidance on musculoskeletal outcomes, consistent with the known vulnerability of this population to accelerated bone loss following iatrogenic menopause (6,22,50). Similarly, positive feedback regarding recipe simplicity, nutritional clarity and practical utility demonstrates that knowledge translation is maximised when interventions balance evidence-based recommendations with flexibility and real-world applicability (51,52). These findings resonate with broader literature on adult learning and digital health interventions where usability, visual design, and contextual relevance are key predictors of engagement and uptake (53).

In the context of this chapter, impact is conceptualised as reach, accessibility, and engagement with evidence-based dietetic information among an underserved survivorship population. While clinical and behavioural outcomes were not assessed, high levels of engagement across multiple formats suggest meaningful intermediate outcomes, including increased exposure to credible nutrition information and integration of dietetic content into survivorship pathways. Critically, while the project demonstrates feasibility and reach, its outcomes also highlight broader systemic gaps in survivorship nutrition care. The lack of integrated guidance in standard oncology

and survivorship frameworks underscores the need for formal recognition of menopause-specific dietary needs, potentially informing future clinical pathways, guidelines, and policy. Furthermore, the results suggest that multimodal delivery, combining printed, digital, and audiovisual formats, may enhance accessibility and inclusivity, supporting diverse learning styles and technological preferences, a principle increasingly advocated in health education and eHealth interventions. These indicators of engagement and utilisation represent important intermediate outcomes in the development of complex survivorship interventions and are necessary precursors to testing behavioural or clinical effectiveness in future trials.

From a theoretical perspective, the project contributes to the emerging field of personalised survivorship nutrition, providing a model that aligns dietary interventions with physiological, symptomatic, and psychosocial dimensions of health. By mapping ingredients to symptom-specific outcomes and aligning recipes with the principles of the Mediterranean Diet the intervention exemplifies how evidence-based nutrition can be operationalised within a patient-centred, multimodal educational framework. The focus on experiential learning and symptom-specific guidance may also have implications for behaviour change research, highlighting pathways to enhance dietary adherence in populations with complex health needs.

In summary, this project demonstrates that it is feasible to develop tailored, multimodal, evidence-informed dietary resources that address the unmet needs of women experiencing iatrogenic menopause. The integration of rigorous literature review, iterative stakeholder consultation, and patient-informed insights has created a resource that is both scientifically credible and highly relevant to end-users, providing a template for future interventions in this and other high-need survivor populations.

Despite its innovations, this project has several limitations. First, the materials were developed and disseminated within an Irish healthcare context, which may limit generalisability to other cultural or service settings. Second, as the primary focus of this chapter was resource development and dissemination, no control or comparison group was included, and funding constraints precluded formal evaluation of behavioural or clinical outcomes. While engagement metrics and qualitative feedback indicate acceptability and perceived utility, the impact on long-term dietary behaviour, symptom management, or clinical endpoints remains untested. Additionally, participation in the webinar series and provision of feedback may reflect selection bias, as individuals who engaged were likely more motivated or health-engaged than the broader survivor population. Finally, minor editorial inconsistencies may exist, as no professional editor was employed.

Future research should build on the development and dissemination work presented in this chapter by evaluating the clinical and behavioural efficacy of The *Menopause Plate* © dietary model through well-powered randomised controlled trials. Such trials should assess outcomes including dietary adherence, symptom burden, musculoskeletal and metabolic health, and quality of life. Further research is also warranted to explore adaptation of the resource across diverse cultural contexts and healthcare systems, its integration into standard survivorship pathways, and associated cost-effectiveness. Finally, investigation of digital engagement strategies and behaviour change mechanisms within multimodal nutrition interventions may help optimise reach, accessibility, and sustained impact for survivors experiencing iatrogenic menopause.

7.7 CONCLUSION

The nutrition-specific needs of cancer survivors impacted by iatrogenic menopause remain largely unmet in current clinical guidance. *Menopause, Diet and Cancer* represents the first multimodal, evidence-informed attempt to address these needs, integrating expert review, patient co-design, and accessible delivery formats. Engagement metrics demonstrate both relevance and acceptability while the symptom-focused, practical approach provides a model for embedding dietetic care within survivorship clinics. Continued collaboration among researchers, clinicians, and survivor communities will be essential to advancing personalised nutrition in cancer survivorship, bridging current gaps in care, and improving long-term health outcomes for women affected by iatrogenic menopause.

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CHAPTER 8: GENERAL DISCUSSIONS AND CONCLUSION

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8.1 GENERAL DISCUSSION

This thesis examined supportive care needs and dietetic service delivery for women surviving early-stage hormone receptor-positive breast and gynaecologic cancers, with a particular focus on survivorship following iatrogenic menopause. This discussion synthesises findings across the programme of research to address the broader question of how dietetic care can be better conceptualised, assessed, and delivered in survivorship.

Five interrelated themes emerged from this work: (1) fundamental gaps in nutritional screening approaches for this population; (2) a symptom-nutrition-supplement triad that challenges conventional interpretations of dietary quality; (3) the role of the LYSA model as a symptom-inclusive, multidisciplinary framework for survivorship care; (4) the need for co-designed, evidence-informed dietetic interventions and resources in the absence of structured guidance; and (5) the implications of these findings for survivorship pathways, dietetic practice, and multidisciplinary care. Collectively, these findings move beyond identifying unmet needs to propose mechanisms, models, and practical directions for improving survivorship dietetic care.

A central finding of this thesis is that commonly used nutritional screening tools inadequately capture risk in women with breast and gynaecologic cancer experiencing iatrogenic menopause. Tools such as the Malnutrition Screening Tool (MST) and body mass index (BMI) detect acute undernutrition but fail to reflect survivorship-specific risks, including treatment-related weight gain, sarcopenic obesity, and symptom-driven dietary compromise. BMI, in particular, cannot differentiate lean from fat mass or identify sarcopenic obesity, limiting its utility in this population. Data from the LYSA Trial highlight this gap: fewer than 10% of participants were classified as at

nutritional risk by the MST at baseline, despite many reporting weight gain, weight-related concerns, and menopausal symptoms affecting dietary intake. While traditional definitions of nutritional risk, as outlined by ESPEN and GLIM criteria (1,2) focus on undernutrition, weight loss, and reduced intake, this research shows that survivorship-related risk also encompasses weight gain, adverse changes in body composition, sarcopenic obesity, and symptom-mediated dietary compromise, all of which can impair quality of life and function (3).

Conventional screening tools therefore overlook survivorship-related nutritional risk in this cohort. For example, using BMI as a trigger classified approximately 60% of participants as having a nutritional issue, yet failed to identify those within a "healthy" BMI range experiencing progressive weight gain. This undernutrition-focused approach likely reflects historical emphasis on acute treatment toxicity and recurrence risk, as well as the normalisation of weight gain during endocrine therapy (4). This misalignment has cascading effects. When nutritional risk is missed, dietetic referral is less likely, leaving survivors to self-manage complex symptom- and weight-related concerns without evidence-based guidance. These findings underscore the need to reconceptualise nutritional screening in survivorship as a dynamic process integrating symptom burden, body composition, and functional status alongside traditional anthropometric measures.

Symptom-integrated screening approaches, incorporating electronic patient-reported outcomes (ePROs) alongside objective measures, offer a more appropriate framework for this population. The LYSA model demonstrates the feasibility of using symptom triggers to prioritise dietetic input, supporting a shift toward dynamic, longitudinal screening that reflects the fluctuating nature of survivorship risk. Such approaches align with emerging survivorship literature advocating for personalised, needs-based

care (5–7) and provide a foundation for more targeted, equitable dietetic service delivery.

Across this body of work, dietary quality, symptom burden, and supplement use consistently emerged as interconnected rather than independent phenomena. A key contribution of this thesis is the demonstration that low dietary quality scores among breast and gynaecologic cancer survivors often reflect adaptive, symptom-driven food choices rather than poor nutritional knowledge, motivation, or engagement. In the LYSA Trial, overall dietary quality adherence was low, with participants in both study arms meeting less than 50% of total adherence scores. Notably, total symptom trigger count was negatively correlated with dietary quality adherence, suggesting that higher symptom burden was associated with lower adherence to conventional dietary metrics. This finding challenges traditional interpretations of dietary quality in survivorship, particularly when assessment tools penalise food avoidance or modification that is undertaken to manage menopausal symptoms or the late effects of cancer treatments.

Current dietary quality metrics, including those aligned with World Cancer Research Fund (WCRF) recommendations, are not symptom-sensitive and lower adherence scores may reflect the limitations of the tools themselves rather than true dietary inadequacy. This has important implications for both clinical interpretation and research outcomes as it risks framing survivorship nutrition challenges as behavioural failings rather than responses to treatment-related physiological change. Similarly, dietary supplement use appears to function as a compensatory self-management strategy. Findings from Chapters 5 and 6 demonstrated high prevalence of supplement use, poly-supplementation, and frequent use of herbal products outside guideline

recommendations, often associated with symptom burden, lower quality of life, and reliance on non-professional information sources. Low dietary quality, high supplement use, and non-disclosure to healthcare professionals form a coherent triad reflecting unmet needs, limited dietetic access, and gaps in guidance.

These findings suggest that survivorship dietetic assessment must move beyond static dietary scores to integrate symptom context, supplement behaviours, and patient priorities. Flexible, symptom-responsive models, such as Mediterranean-style dietary patterns, may better support quality of life and promote benefits for body composition, metabolic health, cardiovascular function, cognitive performance, and menopausal symptoms (8,9). Furthermore, standardised, validated tools adapted to this population are lacking, and their development should consider individual dietetic goals, prescribed therapy, and symptom burden. Dietetic assessment must also be interpreted with nuance, recognising the life-changing impact of cancer and the constraints of fear, anxiety, and symptom burden. Survivors often prioritise symptom control, functionality, and maintaining normality over externally imposed dietary ideals. Approaches that acknowledge adaptive behaviours provide clinically meaningful interpretations of nutritional adequacy, avoid misrepresenting risk, and reinforce patient-centred care.

These findings converge in the LYSA model, which provides an integrative framework for addressing nutritional risk, symptom burden, and survivorship care gaps. Beyond feasibility, the LYSA Trial demonstrates how survivorship care can be reoriented around symptom-responsive, multidisciplinary, dietitian-led models that reflect lived experiences. A defining feature is the central role of symptoms in triggering assessment and intervention: embedding electronic patient-reported

outcomes (ePROs) enables dynamic, individualised prioritisation of support, overcoming limitations of conventional screening and dietary quality metrics.

Importantly, the LYSA model highlights the value of dietitians as key coordinators of survivorship care while also exposing the limitations of siloed interventions. Although dietitian-led consultations were acceptable and associated with improvements in psychosocial outcomes and reduced weight gain concern, the trial also demonstrated that dietetic care cannot be delivered in isolation. Weight gain, body composition change, fatigue, and functional decline are multifactorial phenomena that extend beyond dietary intake alone. The persistence of weight gain concern among participants receiving endocrine therapy, despite stable body composition measures, underscores the need for broader multidisciplinary input.

These findings support the integration of allied health professionals, particularly physiotherapists, within survivorship models. Emerging literature highlights the role of resistance training and physical activity in mitigating sarcopenic obesity (10), preserving function (11), and supporting metabolic health (12) in breast and gynaecologic cancer survivors. The absence of routine body composition monitoring and functional assessment within standard survivorship pathways represents a missing link that limits the effectiveness of dietary intervention alone. Furthermore, in an umbrella reviews of reviews, solo dietary programs were consistently outperformed by multicomponent interventions combining diet with physical activity and psychosocial support (13). Given this, within future iterations of the LYSA model dietetic care should therefore be embedded within a multidisciplinary team (MDT) model that includes physiotherapy, psychosocial, and medical expertise allowing for

coordinated, effective and resource-efficient management of weight, function, and symptom burden.

From an implementation perspective, the LYSA Trial also exposed practical challenges relevant to scalability and sustainability. Dietitian-led consultations were resource-intensive, and the concurrent delivery of nurse-led symptom management and dietetic counselling may have required participants to prioritise acute symptom control over longer-term dietary behaviour change. This finding aligns with implementation science literature demonstrating that intervention intensity must be carefully matched to symptom load and patient capacity (14–16). Future iterations of the LYSA model may benefit from staged or adaptive delivery with dietetic input timed to periods of greatest readiness and symptom stability. Collectively, the LYSA model represents a shift from episodic, problem-focused survivorship care toward a proactive, symptom-inclusive and multidisciplinary framework. By integrating ePRO-driven screening with personalised dietetic input, and coordinated multidisciplinary-based care, the LYSA model provides a scalable template for survivorship care that is responsive to both clinical risk and patient experience.

A consistent theme across this thesis is the absence of structured, evidence-based nutritional guidance for women experiencing iatrogenic menopause following breast or gynaecologic cancer. While survivorship guidelines in Europe acknowledge the importance of lifestyle and supportive care (17,18), they offer limited practical direction for symptom-driven nutritional management and provide minimal guidance for clinicians operating in resource-constrained settings. In this context, survivors are frequently left to navigate complex dietary and supplement-related decisions independently. Guidance from American Cancer Society (5) and the Clinical

Oncology Society of Australia (19) are moving towards a tumour-specific, symptom responsive multidisciplinary model, however European guidelines lack structured guidance.

In response to these gaps, the final component of this research focused on the development of a co-designed, multimodal dietary model tailored to the needs of this survivorship population. Grounded in the empirical findings of this thesis and informed by patient and multidisciplinary expert input the model was designed to translate evidence into practical, symptom-responsive guidance. This approach reflects an intentional shift from identifying unmet needs to addressing the implementation gap between survivorship evidence and real-world care.

The *Menopause Plate* © and its accompanying resources were explicitly developed to acknowledge symptom burden as a central determinant of dietary behaviour. Rather than promoting prescriptive dietary rules, the model offers structured yet adaptable guidance to support management of fatigue, vasomotor symptoms, musculoskeletal pain, gastrointestinal disturbance and cognitive changes. In doing so, it directly addresses the limitations of existing dietary quality and survivorship frameworks and nutritional guidelines which often lack sensitivity to symptom-driven dietary adaptations and may inadvertently misclassify necessary coping strategies as suboptimal dietary behaviour.

The scale of engagement with the co-designed resources highlights both the demand for and acceptability of this approach. Despite limited funding, national dissemination of the *Menopause, Diet and Cancer* resource reached thousands of survivors, with substantial uptake across print, webinar, and digital formats. This level of engagement reinforces the earlier findings of this thesis: survivors are actively seeking information

and support, and when evidence-based, symptom-relevant resources are made accessible, they are readily utilised.

Beyond direct patient benefit the co-designed model also serves an important educational function for clinicians. In healthcare settings where specialist dietetic services are unavailable the resources provide medics and nurses with practical, evidence-informed guidance to support survivorship discussions. Similarly, community dietitians without oncology-specific training are offered a framework for delivering safe, symptom-responsive care to cancer survivors in general practice settings. In this way, the model bridges the gap between specialist oncology knowledge and community-based survivorship care. Importantly, the development of this model should not be viewed as a substitute for comprehensive dietetic services but rather as an enabling strategy within a broader survivorship framework. By supporting informed decision-making, reducing reliance on unverified sources, and facilitating dialogue between survivors and healthcare professionals, co-designed resources represent a critical first step toward more equitable and integrated survivorship nutrition care. When embedded within digital platforms such as the LYSA model, these resources have the potential to enhance continuity, scalability, and consistency of care across the survivorship trajectory.

The findings of this thesis have clear and actionable implications for the organisation and delivery of survivorship care for women experiencing iatrogenic menopause. Collectively, this work challenges existing assumptions regarding nutritional risk, dietary quality, and self-management behaviours in cancer survivorship, and supports a shift toward symptom-responsive, multidisciplinary, and dietitian-integrated models of care.

8.2 IMPLICATIONS AND DIRECTIONS FOR FUTURE RESEARCH

Building on these findings, future research should address the key gaps identified in this thesis, including the development of symptom-responsive screening approaches, evaluation of multidisciplinary interventions, and generation of evidence-based guidance for supplement use and dietary adaptation in survivorship care. Among the research directions identified, the most urgent priorities are redefining nutritional risk in survivorship and evaluating symptom-responsive, multidisciplinary models of dietetic care. These foundational issues determine whether survivors are appropriately identified, referred, and supported, and therefore underpin all subsequent intervention and implementation research.

8.2.1 Reframing Nutritional Screening and Risk Identification in Survivorship

Current survivorship pathways predominantly use screening tools designed to detect acute undernutrition, which systematically under-recognises risks common in breast cancer survivorship, including treatment-related weight gain, adverse body composition changes, sarcopenic obesity, and symptom-driven nutritional compromise. Tools such as the MST and BMI, when used alone, lack the sensitivity and specificity needed to guide dietetic referral and prioritisation in this context.

These findings support reconceptualising nutritional screening as a dynamic, longitudinal process rather than a single point-in-time assessment. Integrating symptom burden, functional status, and weight trajectory, which are supported by electronic patient-reported outcomes and objective measures where feasible, would enable earlier identification of clinically meaningful risk and more targeted allocation of dietetic resources. Future research should focus on developing and validating

survivorship-specific screening and prioritisation tools that reflect this broader understanding of nutritional risk.

A stratified model of care incorporating digital platforms and patient-initiated follow-up may provide a practical implementation strategy. Survivors consistently report a preference for flexible, multimodal dietetic support (20–22). Tumour- or treatment-specific survivorship pathways, delivered through multimodal formats and aligned with the LYSA model, offer a scalable approach for prioritising dietetic input in resource-constrained settings. Evaluation through implementation and health services research, including cost-effectiveness and workforce considerations, remains a key priority.

8.2.2 Interpreting Dietary Quality Through a Symptom-Responsive Lens

A key implication of this research is the need to reinterpret dietary quality in the context of treatment-related symptom burden. Low adherence to conventional dietary quality metrics should not be automatically interpreted as poor dietary behaviour or disengagement, particularly among women experiencing iatrogenic menopause. Instead, dietary modification and food avoidance often represent adaptive strategies to manage symptoms such as gastrointestinal disturbance, vasomotor symptoms, fatigue, and musculoskeletal pain.

For clinical practice, this highlights the importance of using dietary assessment tools that are sensitive to symptom-driven adaptations, or interpreting existing tools with caution. Flexible dietary frameworks, such as Mediterranean-style dietary patterns, may be more appropriate for survivorship care, as they support metabolic health, inflammation reduction, and quality of life without imposing rigid adherence criteria that fail to reflect lived experience. Future intervention trials should explicitly evaluate

symptom-responsive dietary approaches and their effects on both clinical and psychosocial outcomes.

8.2.3 Normalising Supplement Assessment and Guidance in Survivorship Care

High and heterogeneous supplement use emerged as a consistent finding across this research programme, largely driven by symptom burden, unmet supportive care needs, and limited access to professional guidance. These findings underscore the importance of routinely assessing supplement use as an integral component of survivorship nutrition care. Dietitians are well positioned to lead structured supplement assessment, identify potential risks and interactions, and provide evidence-based guidance tailored to symptom profiles and treatment context.

Non-disclosure of supplement use was common and shaped by perceived disinterest, lack of opportunity, and fear of judgement. Creating routine, non-judgemental opportunities for discussion is therefore essential to supporting safe self-management and reducing reliance on unverified information sources. Future research should examine the safety, efficacy, and interaction profiles of commonly used supplements, particularly herbal and botanical products, and evaluate structured approaches to supplement counselling within multidisciplinary survivorship pathways, potentially supported by digital decision-support tools.

8.2.4 Leveraging Digital and Co-Designed Resources to Enhance Access and Equity

Digital health models and co-designed educational resources offer practical strategies to address workforce constraints and inequities in access to specialist dietetic services. The LYSA model and The *Menopause Plate* © demonstrate how symptom-responsive nutritional guidance can be delivered at scale, supporting patient self-efficacy while also providing clinicians with accessible, evidence-informed tools. These resources

should be viewed as complementary to, rather than replacements for, specialist dietetic care. When embedded within digital survivorship platforms, such tools can support stepped-care approaches, enhance continuity, and extend evidence-based guidance to community and primary care settings where oncology-specific dietetic expertise may be limited (22–24). Future implementation research should evaluate the acceptability, scalability, and equity impacts of these approaches, with particular attention to digital access, health literacy, and underserved survivorship populations.

8.2.5 Embedding Dietitians Within Multidisciplinary Survivorship Pathways

This thesis reinforces the central role of dietitians in survivorship care while highlighting the limitations of delivering dietetic interventions in isolation. Weight gain concern, fatigue, adverse body composition change, and functional decline are multifactorial and intersect with physical activity, psychosocial wellbeing, and long-term endocrine therapy. The findings support embedding dietitians within multidisciplinary teams that include nursing, physiotherapy, and psychosocial services. Moving away from fragmented referral-based models toward coordinated survivorship pathways may improve functional and psychosocial outcomes, particularly for survivors receiving adjuvant endocrine therapy who often fall between oncology follow-up and community services (7,25,26). While MDT survivorship care is recommended within existing frameworks, it remains inconsistently implemented. Future research should therefore evaluate MDT survivorship models, including longer-term follow-up to assess impacts on clinical outcomes, healthcare utilisation, and quality of life, to inform policy development and guideline integration.

8.3 STRENGTHS AND LIMITATIONS

Several strengths and limitations should be considered when interpreting the findings of this thesis. A key strength is the use of a multi-method research programme integrating feasibility testing, process evaluation, observational analyses, and co-designed intervention development. This approach enabled both depth and breadth of insight into survivorship dietetic care, while ensuring that findings were grounded in clinical reality and patient experience.

However, several limitations warrant acknowledgement. The LYSA Trial was designed as a feasibility study and was not powered to detect definitive changes in clinical outcomes such as body composition, dietary quality or symptom burden. As a result, causal inferences regarding the effectiveness of the intervention cannot be made. Nonetheless, the trial provides important proof-of-concept evidence regarding acceptability, engagement, and the operationalisation of symptom-responsive, dietitian-led survivorship care.

Many outcomes across the programme of research relied on self-reported measures, including dietary intake, supplement use, symptom burden and quality of life. While validated tools were used where available self-report data are subject to recall bias and social desirability bias, particularly in the context of health behaviours. Similarly, supplement use data may have been under-reported due to non-disclosure or uncertainty regarding product composition, particularly for herbal and botanical products.

Participant demographics were relatively homogeneous, with limited ethnic and socioeconomic diversity, which may restrict the generalisability of findings to more diverse survivorship populations. Digital access and literacy may also have influenced

participation and engagement with the LYSA intervention, potentially excluding survivors with limited access to or familiarity with digital health tools. These factors highlight the need for caution when extrapolating findings to broader populations.

From a service delivery perspective, the resource-intensive nature of dietitian-led interventions presents challenges for scalability and sustainability, particularly in under-resourced health systems. While the LYSA model demonstrates feasibility, implementation at scale would require workforce planning, economic evaluation, and consideration of alternative or stepped-care delivery models. Finally, while this research explored supplement use, the safety and efficacy of many commonly used supplements remain under-researched, limiting the ability to provide definitive clinical recommendations.

8.4 CONCLUSION

This thesis demonstrates the feasibility, acceptability, and potential impact of symptom-responsive, dietitian-led survivorship care for women surviving breast and gynaecologic cancers, particularly those experiencing iatrogenic menopause. Through a comprehensive programme of research, this work identifies critical gaps in nutritional screening, dietary assessment and supplement guidance, while highlighting the central role of symptoms in shaping survivorship nutrition behaviours and dietetic care needs.

By integrating digital ePRO-driven models, multidisciplinary perspectives, and co-designed dietary resources this thesis advances a more nuanced and clinically meaningful approach to survivorship dietetic care. The findings challenge conventional interpretations of dietary quality and nutritional risk, emphasising the need for symptom-inclusive assessment, personalised support and coordinated

multidisciplinary care. Importantly, this work illustrates how evidence-informed, co-designed resources can translate research findings into scalable, real-world solutions that enhance patient empowerment and clinician capacity.

Collectively, the research provides a framework for rethinking how dietetic care is conceptualised and delivered in survivorship. By prioritising symptom burden, embedding dietetic expertise within multidisciplinary pathways, and leveraging digital and educational tools, survivorship care can better align with the lived experiences and long-term needs of cancer survivors. This thesis therefore contributes to the growing evidence base supporting patient-centred, equitable, and responsive survivorship models, with clear implications for future research, clinical practice, and policy development.

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APPENDICES

CHAPTER 3 SUPPLEMENTARY MATERIAL

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Supplementary File: Clinical Research Ethics Committee Responses

COISTE EITICE UM THAIGHDE CLINICIÚIL

Clinical Research Ethics Committee of the Cork Teaching Hospitals

Tel: +353-21-4901901
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University College Cork
Lancaster Hall
6 Little Hanover Street
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CREC Review Reference Number: ECM 4 (y) 20/10/2020
& ECM 3 (ddd) 08/12/2020

Date: 1st December 2020

Professor Roisin Connolly
Chair in Cancer Research
University College Cork
Western Gateway Building
4.110
Western Road
Cork

Study Title: WHI19CON: Women's cancer survivorship: supporting and innovating for change.

Dear Professor Connolly

The following documents have been approved:

- Cover Letter dated 26th November 2020
- Study Protocol Version 3.0 dated 26th November 2020
- Patient Information Leaflet/Informed Consent Form Version 2.0 dated 26th November 2020
- HCP Information and Consent Form for Interview/Focus Group Version 1.0 dated 24th November 2020
- Interview Guide Version 1 dated 3rd November 2020.

Full approval is now granted to carry out the above study. The date of this letter is the date of authorization of the study.

The date of this letter is the date of authorization of the study.

Please keep a copy of this signed approval letter in your study master file for audit purposes. The study must be carried out in accordance with General Data Protection Regulation and Health Research Regulation 2018.

You should note that ethical approval will lapse if you do not adhere to the following conditions:

1. Submission of an Annual Progress Report/Annual Renewal Survey (due annually from the date of this approval letter). **We would encourage you to keep note of this date as the CREC will not issue a reminder.**

2. Report unexpected adverse events, serious adverse events or any event that may affect ethical acceptability of the study

3. Submit any change to study documentation (minor or major) to CREC for review and approval. Amendments must be submitted on an amendment application form and revised study documents must clearly highlight the changes and contain a new version number and date. Amendments cannot be implemented without written approval from CREC.

4. Notify CREC of discontinuation of the study

5. Submit an End of Trial Declaration Form and Final Study Report/Study Synopsis when the study has been completed.

COISTE EITICE UM THAIGHDE CLINICIÚIL

Clinical Research Ethics Committee of the Cork Teaching Hospitals

Tel: +353-21-4901901
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University College Cork
Lancaster Hall
6 Little Hanover Street
Cork
Ireland

CREC Review Reference Number: ECM 4 (y) 20/10/2020
& ECM 3 (kkk) 14/02/2023

Date: 25th January 2023

Professor Roisin Connolly
Chair in Cancer Research
University College Cork
Western Gateway Building
4.110
Western Road
Cork

Study Title: WHI19CON: Women's Cancer Survivorship: The LYSA (Linking You to Support and Advice) Trial.

Dear Professor Connolly

The following documents have been approved:

- Cover Letter dated 16th January 2023
- Amendment Application Form signed 16th January 2023
- Study Protocol Version 9 dated 6th January 2023.

However, full approval is ***not*** granted to implement this amendment. The application will be reviewed again on receipt of the revised participant information leaflet/informed consent form and revised data protection notice.

Yours sincerely

Professor David Kerins
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

Supplementary Table 3.1: Baseline Sociodemographic Characteristics

Characteristic	N	Overall N = 200	Active Comparator N = 98	Experimental N = 102
Sociodemographic Information				
What is your civil status?	193			
Married		118 (61%)	54/95 (57%)	64/98 (65%)
Single		29 (15%)	17/95 (18%)	12/98 (12%)
Cohabiting		15 (7.8%)	5/95 (5.3%)	10/98 (10%)
Separated		11 (5.7%)	7/95 (7.4%)	4/98 (4.1%)
Widowed		11 (5.7%)	6/95 (6.3%)	5/98 (5.1%)
Divorced		9 (4.7%)	6/95 (6.3%)	3/98 (3.1%)
*Which of the following best describes you? **	193			
White Irish		177 (92%)	86/95 (91%)	91/98 (93%)
Any other white background		14 (7.3%)	8/95 (8.4%)	6/98 (6.1%)
Any other Asian background		1 (0.5%)	0/95 (0%)	1/98 (1.0%)
Chinese		1 (0.5%)	1/95 (1.1%)	0/98 (0%)
Which best describes your current living arrangements?	193			
Living with family		93 (48%)	46/95 (48%)	47/98 (48%)
Living with partner		60 (31%)	24/95 (25%)	36/98 (37%)
Living alone		33 (17%)	21/95 (22%)	12/98 (12%)
Living with others		3 (1.6%)	1/95 (1.1%)	2/98 (2.0%)
Other (please specify)		4 (2.1%)	3/95 (3.2%)	1/98 (1.0%)
Do you regularly take care of ill, disabled, elderly relatives/friends aged 15 years of age or more?	*193*			
No		160 (83%)	84/95 (88%)	76/98 (78%)
Yes		33 (17%)	11/95 (12%)	22/98 (22%)
What is your level of education?	193			
None at all		1 (0.5%)	0/95 (0%)	1/98 (1.0%)
Primary level		5 (2.6%)	2/95 (2.1%)	3/98 (3.1%)
Secondary level		62 (32%)	32/95 (34%)	30/98 (31%)
Third level (college/university)		125 (65%)	61/95 (64%)	64/98 (65%)
Before cancer diagnosis, which of these descriptions best describes your household?	*193*			
Living comfortably on present income		108 (56%)	54/95 (57%)	54/98 (55%)
Coping on present income		67 (35%)	33/95 (35%)	34/98 (35%)
Difficult on present income		8 (4.1%)	4/95 (4.2%)	4/98 (4.1%)
Very difficult on present income		6 (3.1%)	3/95 (3.2%)	3/98 (3.1%)
Rather not say		4 (2.1%)	1/95 (1.1%)	3/98 (3.1%)
At the moment, which of the following best defines your economic status?	*193*			

Unable to work due to sickness or disability		68 (35%)	35/95 (37%)	33/98 (34%)
Employed		57 (30%)	26/95 (27%)	31/98 (32%)
Retired		34 (18%)	17/95 (18%)	17/98 (17%)
Looking after home/family		19 (9.8%)	8/95 (8.4%)	11/98 (11%)
Unemployed, looking for a job		4 (2.1%)	3/95 (3.2%)	1/98 (1.0%)
Other		4 (2.1%)	3/95 (3.2%)	1/98 (1.0%)
Student		3 (1.6%)	1/95 (1.1%)	2/98 (2.0%)
Unemployed, not looking for a job		3 (1.6%)	2/95 (2.1%)	1/98 (1.0%)
Unable to work due to COVID restrictions		1 (0.5%)	0/95 (0%)	1/98 (1.0%)
Do you smoke regularly?	193			
No		178 (92%)	88/95 (93%)	90/98 (92%)
Yes		15 (7.8%)	7/95 (7.4%)	8/98 (8.2%)
Do you drink alcohol?	193			
No		44 (23%)	21/95 (22%)	23/98 (23%)
Yes		149 (77%)	74/95 (78%)	75/98 (77%)

* Standard reference classification used by the Central Statistics Office (Republic of Ireland)

Supplementary Table 3.2: Thematised Reasons for Study Discontinuation

Theme	Reasons Given for Discontinuation (n=18)
Lost to follow up / declined to come back to hospital	Failed to answer any contact made by research team to complete her end of study virtual dietetic assessment
	Unhappy to travel to the hospital. Did Baseline survey and then did not want to return to CUH. Very nervous with covid initially and then very low mood *
	Declined to attend the hospital for the end of study visit, completed end of study survey and then lost contact with the study
	Patient did not disclose as lost contact with the study
	Did not get to speak with patient in relation to drop out. Did not answer phone calls/texts or complete surveys
	Patient declined to attend the hospital for the 12-month clinical visit due to work commitments *
	Offered to reschedule but patient did not respond
	Declined to complete end of study survey and attend End of study hospital visit
	Did not complete two consecutive surveys
Comorbidities	Unwell with comorbidity (Ulcerative colitis)
	Due to comorbidities, she finds coming to the hospital difficult, wheelchair user
	Ongoing comorbidity, multiple hospital appointments around this. Mood low at present- recently changed antidepressants by GP
IT issues	Daughter unable to help with IT
	Son unable to help with IT
Wanting to move beyond cancer diagnosis	Did not want to be reminded of hospitals or cancer
	Too busy back at work and unable to get time off for clinic visit. Feels well overall
	Too busy to do the study
	Personal decision
Change to treatment plan	Not meeting eligibility, not on/going on endocrine therapy
Dissatisfaction with randomisation	Part of control group, not happy with same

* Some reasons articulated cross multiple themes reflecting the complex factors influencing participation in supportive care interventions.

Abbreviations: CUH, Cork University Hospital; GP, General Practitioner; IT, Information Technology

Supplementary Table 3.3: Completion Rates for ePRO Symptom Survey Package

Study Timepoint	Active Comparator (n = 98)			Experimental (n = 102)		
	Scheduled	Completed	%	Scheduled	Completed	%
Baseline (T0)	98	95	97	102	98	96
Follow-Up 1 (T2)				102	95	93
Follow-Up 2 (T4)				102	94	92
Follow-Up 3 (T6)				102	92	90
Follow-Up 4 (T8)				102	91	89
Follow-Up 5 (T10)				102	85	83
End of the Study (T12)	98	87	90	102	91	89

Supplementary Table 3.4: LYSA ePRO Trigger Alert Matrix and Example

Instruments	Raw Score	T score equivalence	Colour	Trigger
PRO-CTCAE™ Symptoms Term + Fear of recurrence	0 to 2 or No	-		Trigger for **severity** alert: score ≥3 or increase in score by ≥2 compared to
	3 to 4 or Yes	-		
PROMIS - Fatigue	0-4	Less than 39.7		Trigger for **fatigue** alert: T score ≥ 70 and/or increase in T score of ≥ 5 compared to baseline score
	5 to 11	More than 39.7 to less than 57.0		
	12 to 18	Equal to 57.0 and less than 69		
	More than 18	Equal or more than 69		
PROMIS - Emotional distress- anxiety	0-4	Less than 48		Trigger for Emotional distress – **anxiety** alert: T score ≥ 70 and/or increase in T score of ≥ 5 compared to baseline score
	5 to 11	More than 48 to less 63.4		
	12 to 15	Equal to 63.4 and less than 70		
	More than 15	Equal or more than 70		
PROMIS - Emotional distress-depression	0-4	Less than 49.0		Trigger for Emotional distress-**depression** alert: T score ≥ 70 and/or increase in T score of ≥ 5 compared to baseline score
	5 to 11	More than 49.0 to less 62.2		
	12 to 16	Equal to 62.2 and less than 70		
	More than 16	Equal or more than 70		
PROMIS – Vaginal Discomfort	0 to 5	Less than 48.09		Trigger for **vaginal discomfort** alert: T score ≥ 70 and/or increase in T score of ≥ 5 compared to baseline score
	6 to 10	Equal or more than 48.09 to less than 58.56		
	11 to 13	Equal to 58.56 and less than 69.81		
	14	Equal or more than 69.81		

Malnutrition Screening Tool Score	0 to 1	-		Trigger if ≥2
	2 to 7	-		
Body Mass Index and Weight Gain Concern	-	18.5 to less than 25.5		Trigger if: - BMI scores between 25.5 (included) to 30 (included) and they answer “yes” to weight gain concern - BMI more than 30
	-	More than 25.5 to 30 + no weight gain concern		
	-	More than 25.5 to 30 + weight gain concern		
	-	More than 30		
Adherence to hormonal therapy	1 to 3	-		Trigger if ≥4
	4 to 6	-		
Medication changes	No	-		Trigger if “Yes”
	Yes	-		
Use of resources	No	-		Trigger if “Yes”
	Yes	-		
Medical conditions	No	-		Trigger if “Yes”
	Yes	-		
Hospitalisations	No	-		Trigger if “Yes”
	Yes	-		

Abbreviations: BMI, Body Mass Index; PRO-CTCAE, Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events; PROMIS, Patient-Reported Outcomes Measurement Information System

Supplementary Table 3.5: Disease Specific EORTC QLQ Scores

Standardised EORTC-BR23 breast cancer scores at baseline and the end of the study (n = 147)	**N**	**Baseline (T0)**		**N**	**Endpoint (T12)**	
		Control N = 73[1]	**Active** N = 74[1]		**Control** N = 73[1]	**Active** N = 74[1]
EORTC QLQ-BR23 body image score	142	61 (31); 67 [33, 83]	56 (33); 67 [25, 83]	139	70 (29); 75 [50, 100]	65 (28); 67 [50, 83]
Missing values		*2*	*3*		*6*	*2*
EORTC QLQ-BR23 sexual functioning score	142	17 (18); 17 [0, 33]	14 (18); 0 [0, 17]	139	17 (20); 17 [0, 33]	19 (19); 17 [0, 33]
Missing values		*2*	*3*		*6*	*2*
EORTC QLQ-BR23 sexual enjoyment score	55	47 (28); 33 [33, 67]	54 (31); 67 [33, 67]	59	56 (25); 67 [33, 67]	46 (28); 33 [33, 67]
Missing values		*41*	*51*		*48*	*40*
EORTC QLQ-BR23 future perspective score	142	45 (26); 67 [33, 67]	41 (31); 33 [0, 67]	139	45 (29); 33 [33, 67]	54 (30); 67 [33, 67]
Missing values		*2*	*3*		*6*	*2*
EORTC QLQ-BR23 systemic therapy side effects score	142	75 (20); 81 [71, 86]	74 (19); 76 [62, 90]	139	77 (21); 86 [71, 90]	82 (14); 86 [76, 90]
Missing values		*2*	*3*		*6*	*2*
EORTC QLQ-BR23 breast symptoms score	142	74 (20); 75 [67, 83]	71 (20); 75 [58, 83]	139	81 (18); 83 [75, 100]	83 (15); 83 [75, 92]
Missing values		*2*	*3*		*6*	*2*
EORTC QLQ-BR23 arm symptoms score	142	78 (20); 78 [67, 100]	80 (21); 89 [67, 100]	139	80 (24); 89 [67, 100]	82 (15); 78 [78, 100]
Missing values		*2*	*3*		*6*	*2*
EORTC QLQ-BR23 upset by hair loss score	39	33 (34); 33 [0, 67]	45 (41); 67 [0, 67]	21	42 (41); 50 [0, 67]	70 (35); 67 [67, 100]

Missing values		*57*	*51*	*61*	*65*

1 Mean (SD); Median [Q1, Q3]

Standardised EORTC QLQ-CX24 cervical cancer scores at baseline and the end of the study (n = 11)	**N**	**Baseline (T0)**		**End of Study (T12)**	
		Control N = 4*1*	**Active** N = 7*1*	**Control** N = 4*1*	**Active** N = 7*1*
EORTC QLQ-CX24 symptom experience score	11	81 (8); 80 [76, 86]	84 (9); 82 [82, 91]	87 (8); 86 [82, 92]	87 (10); 88 [82, 94]
EORTC QLQ-CX24 body image score	11	72 (21); 67 [56, 89]	67 (29); 67 [33, 89]	72 (33); 78 [44, 100]	73 (32); 89 [56, 100]
EORTC QLQ-CX24 sexual functioning score	2	83 (NA); 83 [83, 83]	58 (NA); 58 [58, 58]	91.7 (NA); 91.7 [91.7, 91.7]	83.3 (NA); 83.3 [83.3, 83.3]
Missing values		*3*	*6*	*3*	*6*
EORTC QLQ-CX24 lymphoedema score	11	83 (19); 83 [67, 100]	86 (18); 100 [67, 100]	100 (0); 100 [100, 100]	81 (26); 100 [67, 100]
EORTC QLQ-CX24 peripheral neuropathy score	11	83 (19); 83 [67, 100]	86 (26); 100 [67, 100]	100 (0); 100 [100, 100]	76 (16); 67 [67, 100]
EORTC QLQ-CX24 menopausal symptom score	11	67 (27); 67 [50, 83]	38 (49); 0 [0, 100]	75 (17); 67 [67, 83]	52 (42); 67 [0, 100]
EORTC QLQ-CX24 sexual worry score	11	75 (32); 83 [50, 100]	57 (46); 67 [0, 100]	75 (32); 83 [50, 100]	76 (37); 100 [67, 100]
EORTC QLQ-CX24 sexual activity score	11	8 (17); 0 [0, 17]	10 (25); 0 [0, 0]	8 (17); 0 [0, 17]	14 (38); 0 [0, 0]
EORTC QLQ-CX24 sexual enjoyment score (baseline)	2	33.3 (NA); 33.3 [33.3, 33.3]	33.3 (NA); 33.3 [33.3, 33.3]	66.7 (NA); 66.7 [66.7, 66.7]	66.7 (NA); 66. 7 [66.7, 66.7]
Missing values		*3*	*6*	*3*	*6*

1 Mean (SD); Median [Q1, Q3]

Standardised EORTC QLQ-EN24 endometrial cancer scores at baseline and the end of the study (n = 13)	N	Baseline (T0)		End of Study (T12)	
		Control	Active	Control	Active
		N = 5[1]	N = 8[1]	N = 5[1]	N = 8[1]
EORTC QLQ-EN24 lymphoedema score	13	80 (30); 100 [67, 100]	85 (30); 100 [83, 100]	70 (25); 67 [67, 83]	90 (13); 100 [83, 100]
Missing values		*0*	*0*	*0*	*1*
EORTC QLQ-EN24 urological symptom score	13	65 (12); 67 [58, 67]	77 (19); 79 [67, 92]	78 (13); 83 [75, 83]	79 (16); 83 [67, 92]
Missing values		*0*	*0*	*0*	*1*
EORTC QLQ-EN24 gastrointestinal symptom score	13	83 (24); 93 [87, 93]	79 (13); 77 [70, 93]	91 (6); 87 [87, 93]	89 (13); 93 [87, 93]
Missing values		*0*	*0*	*0*	*1*
EORTC QLQ-EN24 body image score	13	70 (41); 83 [67, 100]	69 (19); 67 [67, 75]	90 (15); 100 [83, 100]	83 (22); 100 [67, 100]
Missing values		*0*	*0*	*0*	*1*
EORTC QLQ-EN24 sexual problems score (baseline)	5	72 (8); 72 [67, 78]	74 (13); 67 [67, 89]	94 (8); 94 [89, 100]	93 (13); 100 [78, 100]
Missing values		*3*	*5*	*3*	*5*
EORTC QLQ-EN24 back pain score	13	93 (15); 100 [100, 100]	88 (17); 100 [67, 100]	87 (18); 100 [67, 100]	86 (26); 100 [67, 100]
Missing values		*0*	*0*	*0*	*1*
EORTC QLQ-EN24 tingling score	13	87 (18); 100 [67, 100]	63 (45); 83 [17, 100]	53 (38); 67 [33, 67]	67 (38); 67 [33, 100]
Missing values		*0*	*0*	*0*	*1*
EORTC QLQ-EN24 joint pain score	13	87 (18); 100 [67, 100]	71 (21); 67 [67, 83]	67 (41); 67 [67, 100]	71 (30); 67 [33, 100]
Missing values		*0*	*0*	*0*	*1*

EORTC QLQ-EN24 hair loss score	13	40 (55); 0 [0, 100]	63 (52); 100 [0, 100]	73 (43); 100 [67, 100]	100 (0); 100 [100, 100]
Missing values		*0*	*0*	*0*	*1*
EORTC QLQ-EN24 taste change symptom score	13	60 (43); 67 [33, 100]	88 (17); 100 [67, 100]	73 (28); 67 [67, 100]	100 (0); 100 [100, 100]
Missing values		*0*	*0*	*0*	*1*
EORTC QLQ-EN24 sexual interest score	13	20 (30); 0 [0, 33]	13 (17); 0 [0, 33]	27 (37); 0 [0, 67]	19 (26); 0 [0, 33]
Missing values		*0*	*0*	*0*	*1*
EORTC QLQ-EN24 sexual activity score	13	27 (43); 0 [0, 33]	13 (17); 0 [0, 33]	27 (37); 0 [0, 67]	19 (26); 0 [0, 33]
Missing values		*0*	*0*	*0*	*1*
EORTC QLQ-EN24 sexual enjoyment score	5	50 (24); 50 [33, 67]	22 (19); 33 [0, 33]	83 (24); 83 [67, 100]	67 (33); 67 [33, 100]
Missing values		*3*	*5*	*3*	*5*

1 Mean (SD); Median [Q1, Q3]

Supplementary Table 3.6: Usability and Satisfaction Survey

Level of agreement with statements in relation to participant experience of using the web-based system for completing electronic surveys (electronic Patient Reported Outcomes - ePROs). *	**N**	**Overall**		**Active Comparator**		**Experimental Arm**	
		N = 149 (%)		N = 69 (%)		N = 80	
The computer interface (screen layout) was pleasant and user friendly	149						
Disagree		4	*(2.7%)*	2	*(2.9%)*	2	*(2.5%)*
Neither disagree nor agree		5	*(3.4%)*	3	*(4.3%)*	2	*(2.5%)*
Agree		140	*(94.0%)*	64	*(92.8%)*	76	*(95.0%)*
The computer system was simple to use	149						
Disagree		7	*(4.7%)*	3	*(4.3%)*	4	*(5.0%)*
Neither disagree nor agree		5	*(3.4%)*	5	*(7.2%)*	0	*(0.0%)*
Agree		137	*(91.9%)*	61	*(88.4%)*	76	*(95.0%)*
I felt comfortable using the computerised questionnaire system	149						
Disagree		8	*(5.4%)*	4	*(5.8%)*	4	*(5.0%)*
Neither disagree nor agree		5	*(3.4%)*	5	*(7.2%)*	0	*(0.0%)*
Agree		136	*(91.3%)*	60	*(87.0%)*	76	*(95.0%)*
Overall, I was satisfied with completing questionnaires on the computerised system	149						
Disagree		6	*(4.0%)*	3	*(4.3%)*	3	*(3.8%)*
Neither disagree nor agree		5	*(3.4%)*	5	*(7.2%)*	0	*(0.0%)*
Agree		138	*(92.6%)*	61	*(88.4%)*	77	*(96.3%)*
I would prefer to complete computerised versions of questionnaires over paper-based versions	149						
Disagree		45	*(30.2%)*	23	*(33.3%)*	22	*(27.5%)*
Neither disagree nor agree		20	*(13.4%)*	10	*(14.5%)*	10	*(12.5%)*
Agree		84	*(56.4%)*	36	*(52.2%)*	48	*(60.0%)*

The information (such as on-line help, on-screen messages and other documentation) provided within this system was clear	149					
Disagree		3	*(2.0%)*	1	*(1.4%)*	2	*(2.5%)*
Neither disagree nor agree		8	*(5.4%)*	8	*(11.6%)*	0	*(0.0%)*
Agree		138	*(92.6%)*	60	*(87.0%)*	78	*(97.5%)*
In general, the time it took me to complete the computerised questionnaires on the ePRO system was reasonable	149					
Disagree		3	*(2.0%)*	1	*(1.4%)*	2	*(2.5%)*
Neither disagree nor agree		7	*(4.7%)*	5	*(7.2%)*	2	*(2.5%)*
Agree		139	*(93.3%)*	63	*(91.3%)*	76	*(95.0%)*

** Responses from a five-point Likert scale were collapsed into three categories: 'agree' (combining strongly agree and somewhat agree), 'neither disagree nor agree,' and 'disagree' (combining somewhat disagree and strongly disagree).*

Level of satisfaction with core elements of LYSA intervention in the Experimental Arm, over the past 12 months:	**N**	**N = 79 (%)**	
The assessments of my symptoms, quality of life, and diet/nutrition	79		
Disagree		0	*(0.0%)*
Neither disagree nor agree		1	*(1.3%)*
Agree		78	*(98.7%)*
The Treatment Summary and Care Plan I received at the first Clinic visit	79		
Disagree		0	*(0.0%)*
Neither disagree nor agree		1	*(1.3%)*
Agree		78	*(98.7%)*
The information and advice I received to manage my symptoms/concerns	79		
Disagree		0	*(0.0%)*
Neither disagree nor agree		0	*(0.0%)*
Agree		79	*(100.0%)*

The access to the care/services I needed to deal with my symptoms/concerns	79		
Disagree		0	*(0.0%)*
Neither disagree nor agree		6	*(7.6%)*
Agree		73	*(92.4%)*
The timeliness of access to follow-up care/support services I received	79		
Disagree		0	*(0.0%)*
Neither disagree nor agree		8	*(10.1%)*
Agree		71	*(89.9%)*
The level of follow-up support I received from the Clinic's healthcare providers	79		
Disagree		0	*(0.0%)*
Neither disagree nor agree		2	*(2.5%)*
Agree		77	*(97.5%)*
The one-to-one consultation sessions I had with the Clinic's Nurse	79		
Disagree		0	*(0.0%)*
Neither disagree nor agree		0	*(0.0%)*
Agree		79	*(100.0%)*
The one-to-one consultation sessions I had with the Clinic's Dietitian	79		
Disagree		1	*(1.3%)*
Neither disagree nor agree		0	*(0.0%)*
Agree		78	*(98.7%)*
Individualised nutritional advice/counselling I received from the Clinic's Dietitian	79		
Disagree		0	*(0.0%)*
Neither disagree nor disagree		3	*(3.8%)*
Agree		76	*(96.2%)*
Using the computerised system of electronic surveys (ePROs) to collect symptom and quality of life information	79		
Disagree		0	*(0.0%)*
Neither disagree nor agree		2	*(2.5%)*
Agree		77	*(97.5%)*

My overall experience of participating in this Women's Survivorship Study	79		
Disagree		0	*(0.0%)*
Neither disagree nor agree		0	*(0.0%)*
Agree		79	*(100.0%)*
My Personalised Symptom Pathway Plan(s)	79		
Disagree		0	*(0.0%)*
Neither disagree nor agree		2	*(2.5%)*
Agree		77	*(97.5%)*

** Responses from a five-point Likert scale were collapsed into three categories: 'agree' (combining strongly agree and somewhat agree), 'neither disagree nor agree,' and 'disagree' (combining somewhat disagree and strongly disagree).*

Level of satisfaction with core elements of the LYSA Trial in the Active Comparator Arm, over the past 12 months:	**N**	**N = 70**[1] (%)	
The assessments of my symptoms, quality of life, and diet/nutrition	70		
Disagree		3	*(4.3%)*
Neither disagree nor agree		6	*(8.6%)*
Agree		61	*(87.1%)*
The Treatment Summary and Care Plan I received at the first Clinic visit	70		
Disagree		2	*(2.9%)*
Neither disagree nor agree		8	*(11.4%)*
Agree		60	*(85.7%)*
The information and advice I received to manage my symptoms/concerns	70		
Disagree		3	*(4.3%)*
Neither disagree nor agree		7	*(10.0%)*
Agree		60	*(85.7%)*
The access to the care/services I needed to deal with my symptoms/concerns	70		
Disagree		6	*(8.6%)*
Neither disagree nor agree		9	*(12.9%)*
Agree		55	*(78.6%)*

The timeliness of access to follow-up care/support services I received	70		
Disagree		5	*(7.1%)*
Neither disagree nor agree		13	*(18.6%)*
Agree		52	*(74.3%)*
The level of follow-up support I received as part of my usual follow up care	70		
Disagree		3	*(4.3%)*
Neither disagree nor agree		14	*(20.0%)*
Agree		53	*(75.7%)*
Using the computerised system of electronic surveys (ePROs) to collect symptom and quality of life information	70		
Disagree		0	*(0.0%)*
Neither disagree nor agree		9	*(12.9%)*
Agree		61	*(87.1%)*
My overall experience of participating in this Women's Survivorship Study	70		
Disagree		2	*(2.9%)*
Neither disagree nor agree		7	*(10.0%)*
Agree		61	*(87.1%)*

** Responses from a five-point Likert scale were collapsed into three categories: 'agree' (combining strongly agree and somewhat agree), 'neither disagree nor agree,' and 'disagree' (combining somewhat disagree and strongly disagree).*

Supplementary Table 3.7 Positive and negative implementation factors linked to implementation of the LYSA Feasibility Trial organised according to the PRISM (RE-AIM) framework

Dimension *	Definition / Examples in current study	Category (as per process evaluation data)	Positives/Enablers of LYSA Intervention	Negatives/Barriers to LYSA Intervention
Perspectives on the intervention	E.g. history with similar programs and associated services	Intervention	Able to learn from international experience of similar intervention and ePRO monitoring system (shared learning)	Symptom management pathways not fully developed, implemented or resourced for rare symptoms (e.g. peripheral neuropathy, weight management in oncology)
Values and characteristics of Implementing Settings. Multilevel partner, organisational characteristics Implementer characteristics. Patient characteristics	Refers to characteristics that affect organisations' ability to successfully adopt, implement intervention. Refers to characteristics of implementers, their settings, intended patients	Partners and relationships	Strong professional relationships, MDT and partnership between hospital, community organisations, clinical research infrastructure and collaborators at the university. Strong professional relationships between healthcare professionals and patients Access to community-based support centres and structures enabled through signposting Professional respect and enthusiasm for LYSA	Reliant on personal relationships and implementer's knowledge of infrastructure and health care professionals active in cancer survivorship supportive care
External environment- e.g. potential drivers of inequalities	Refers to context of relevant policies, strategies, incentives, regulatory environment and community resources	Enabling national policy and context External influencing factors	Increased national focus on enabling post treatment support for patients with cancer and linking with community-based services	Formal links between community and acute oncology survivorship services not fully developed. LYSA limited to patients with breast and gynaecological cancers Limited digital and English language capabilities impeded participation COVID-19 Cyberattack of Irish health service during study
Implementation and sustainability infrastructure	Refers to characteristics such as adopter training and support, dedicated team for implementation, resources and plans for sustainability.	Implementation, resources and plans for sustainability Infrastructure	Dedicated LYSA team supported through once off funding LYSA deemed feasible Parallel economic evaluation Dedicated staff/human resource Infrastructure- access to clinical space, Castor digital system	Feasibility study- need a full trial Lack of funding and dedicated staff to maintain LYSA LYSA is feasible, problem is meeting the demand Dedicated staff and buy in from organisation and partner services not secured for continued roll out Ability to link university-based research system and clinical systems is

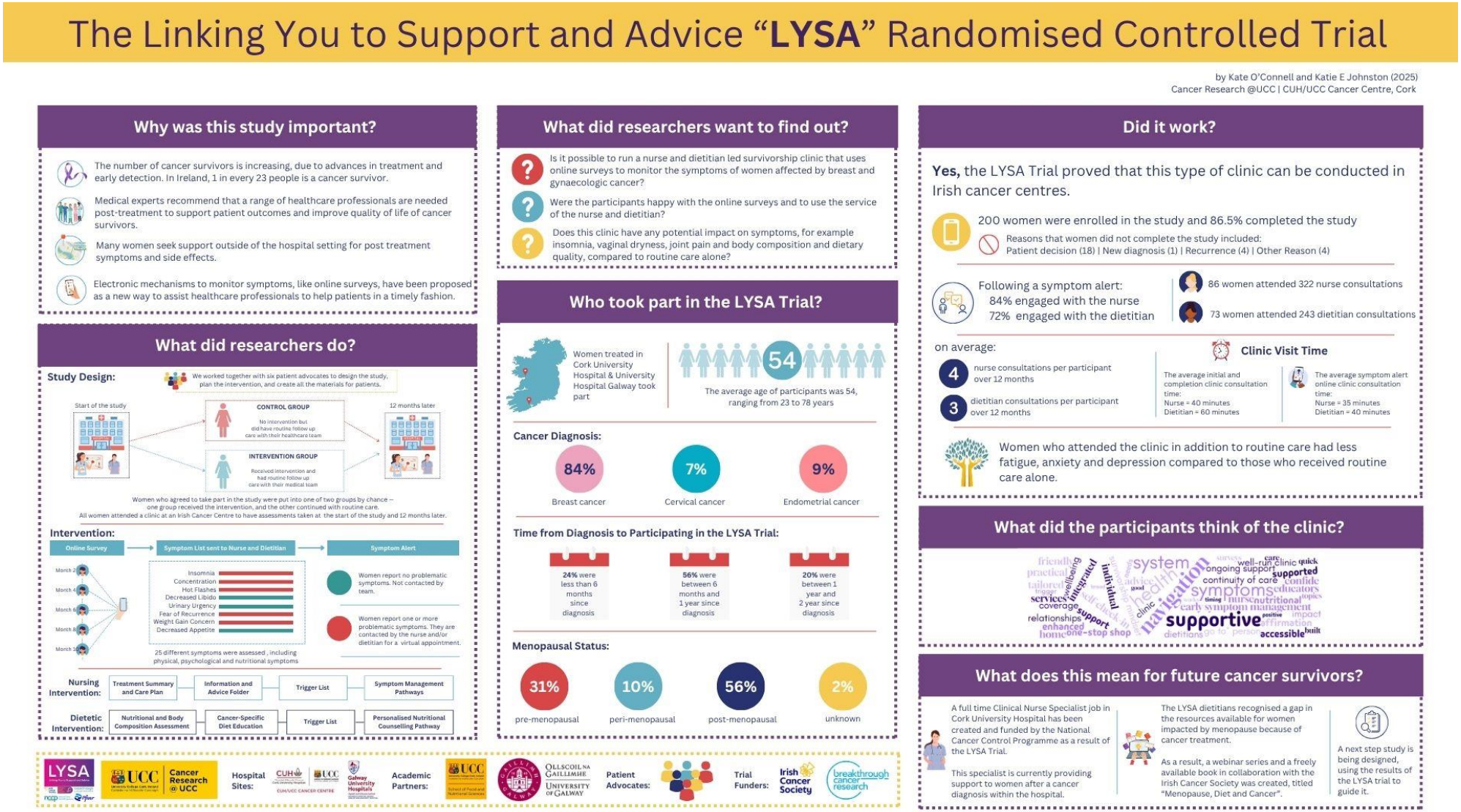
				complex requires data sharing agreements and arrangements
Reach	The number, proportion, and representativeness of individuals who were willing to participate in the LYSA study and intervention	Patient related factors	Motivation to participate	The process of symptom i.e. regular reporting via ePRO, acted as a reminder of cancer adding to psychological distress
		Recruitment to study	Identification of barriers to enrolment early on enhanced recruitment. Engagement of all relevant stakeholders. Public Patient Involvement Virtual/tele connectivity	Initial narrow clinical eligibility criteria. COVID-19 context required adaptations to accrual and consent processes Limited number of patients with gynaecological cancer recruited Limited enrolment of ethnic minorities
		Digital capabilities	Digital capability of participants or supportive person	Limited digital capabilities Didn't have access to paper surveys for those with limited digital access or capability
Effectiveness or efficacy	Positive and negative factors impacting the implementation of the LYSA study and intervention	MDT intervention	Clinical assistance or clinical backup for the nurse led service	Not a 24/7 service Limited psycho-oncology services e.g. access to counselling Lack of fully resourced pathways for rarer symptoms
		Having symptom pathways	Having identified symptom management pathways, referral systems and identified clinic provides a structure to manage symptoms proactively	Dietetic triggers need to be more developed as not meeting the needs or identifying the needs of BMI 18.5kg/m^2 - 25.5 kg/m^2 or BMI <18.5 kg/m^2
		Ethics and reporting processes	Streamlined ethics application and reporting templates and processes for clinical studies across sites	Complexity of ethics applications in multisite studies
		Service level support	Support with logistics Support from clinical and department leaders especially line managers of staff involved Support from hospital leadership team	Difficulties integrating digital intervention into clinical workflow
		Patient level affirmation of the benefits of the intervention through feedback, ePROs and PPI	Positive experiences with clinic (e.g. supportive, accessible, helped with symptoms, good set up, accommodating)	

Adoption	Enablers and barriers to the initial adoption of the intervention among participants + those involved in delivering the intervention	Co-design	Involvement of PPI. Support of the academic and wider research team was an enabler. Steering group of stakeholders. Being part of a broader multicentre "Women's Health Initiative"	
		Being a research study	Research allows learning to be integrated into practice. Ability to get publications is also positive	
Implementation (individual and setting)	Enablers and barriers in implementing the intervention as planned over the two years of the study from recruitment to completion of study	Having a clear study protocol	Team developed protocol Following the protocol very well Being able to make minor changes as needed to the protocol- as the real-world scenario becomes clearer	Implementing a complex intervention in real world settings leads to unanticipated barriers and challenges
Maintenance (individual and setting)	Activities to be executed to sustain the (implementation of the) intervention over time beyond the current study	Funding and resources	Access to funding and resources for staff to support enhanced supportive care clinics and systems Time and resources to manage workload associated with reviewing and responding to survey initiated triggers	Sustainment of a clinical intervention beyond a research study when research funding is limited, and posts are contract posts Embedding research into clinical roles with clinicians having conflicting responsibilities
		Digital infrastructure	Digitally enabled infrastructure- linking to existing systems in the hospital and into the community	Digital infrastructure developed during research is not easily embedded into routine care of the patient outside of the research study Difficulty embedding LYSA digital record into patient records
		Giving live feedback to patient and HCP	Graphs and triggers live to patient and HCP is recommended.	Feedback is not automated- requires HCP response and takes time.

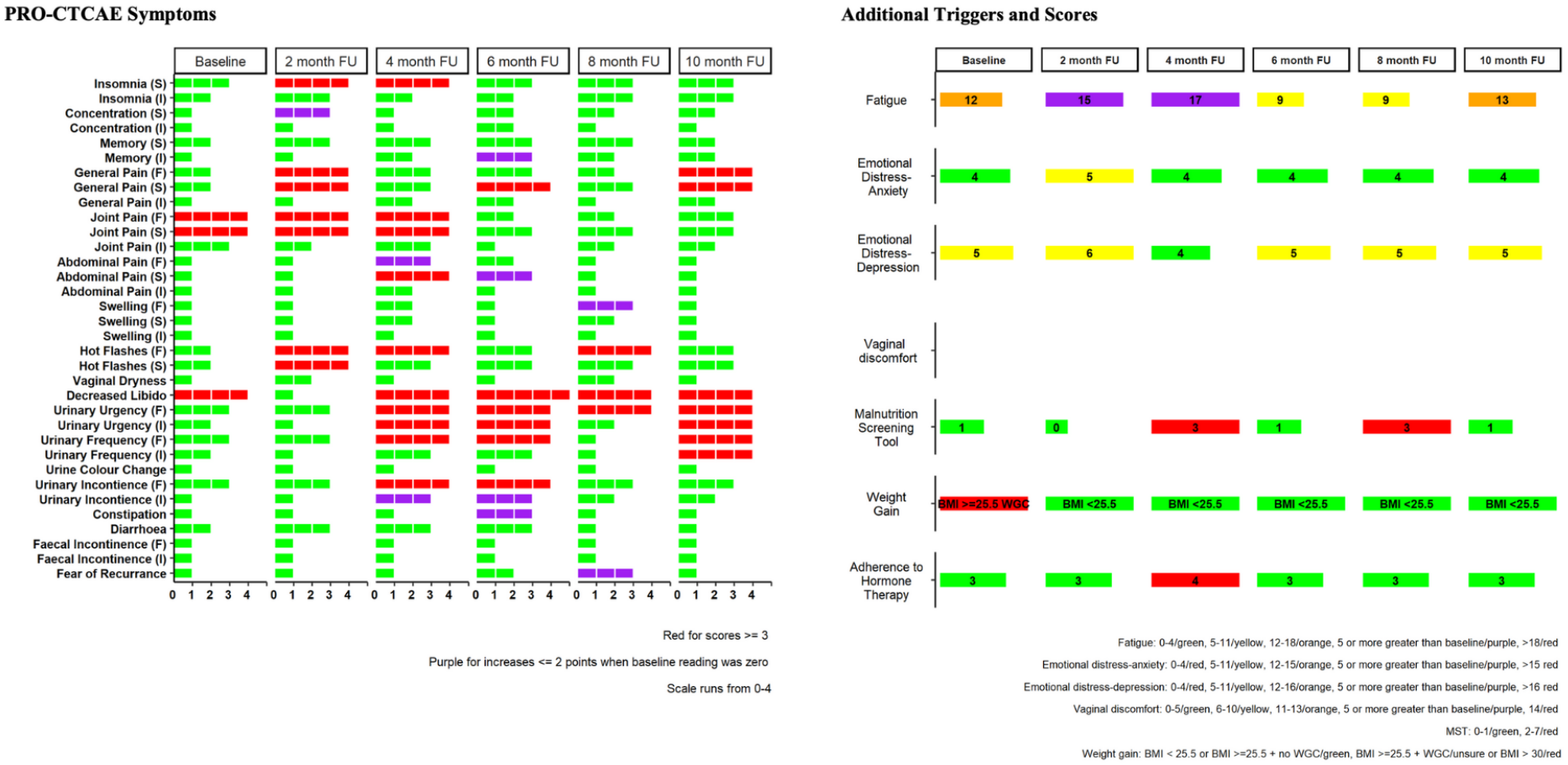
* Deductive analysis was applied in this analysis providing a structured method of analysis that applied predefined themes or dimensions drawn from the PRISM(RE-AIM) framework to the presentation of the qualitative data presented in this table.

Abbreviations: BMI, Body Mass Index; ePROs, electronic Patient Reported Outcomes; HCP, Healthcare Professional; MDT, Multidisciplinary Team; PPI, Patient and Public Involvement

Supplementary Figure 3.1: Lay Summary



Supplementary Figure 3.2: Example of ePRO Trigger List



Abbreviations: PRO-CTCAE - Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events; (S) Severity; (I) Interference; (F) Frequency; FU Follow Up; BMI Body Mass Index; MST Malnutrition Screening Tool; WGC Weight Gain Concern

CHAPTER 4 SUPPLEMENTARY MATERIAL

Supplementary Table 4.1: Operationalisation of a Modified World Cancer Research Fund/American Institute Cancer Research (WCRF/AICR) Standardised Scoring System within the LYSA Trial

Supplementary Table 4.1: Operationalisation of a Modified World Cancer Research Fund/American Institute Cancer Research (WCRF/AICR) Standardised Scoring System within the LYSA Trial

WCRF/AICR Recommendation	Operationalisation of Recommendation	Points	Data Extracted From:
1. Be a healthy weight	**BMI**		Baseline or Endpoint anthropometric data collected by the dietitian
	18.5–24.9	0.5	
	25–29.9	0.25	
	<18.5 or ≥30	0	
	Waist Circumference		Baseline or Endpoint anthropometric data collected by the dietitian
	Women: <80 (<31.5)	0.5	
	Women: 80–<88 (31.5– <35)	0.25	
	Women: ≥88 (≥35)	0	
2. Be physically active	**Total Moderate-Vigorous Physical Activity (minutes / week)**		Question 23 of baseline or endpoint survey
	≥150	1	
	75 – <150	0.5	
	<75	0	
3. Eat a diet rich in wholegrains, vegetables, fruit and beans	**Fruits and vegetables (grams/day):**		Baseline or Endpoint nutritional assessments, including 24-hour recall, WCRF checklist and FFQ
	≥400	0.5	
	200 – <400	0.25	
	<200	0	
	Total fibre (grams/day):		
	≥30	0.5	
	15 – <30	0.25	
	<15	0	
4. Limit consumption of red and processed meat	**Total red meat (grams/week) and processed meat (grams/week):**		Baseline or Endpoint nutritional assessments, including 24-hour recall, WCRF checklist and FFQ
	Red meat <500 and processed meat <21	1	
	Red meat <500 and processed meat 21– <100	0.5	
	Red meat >500 or processed meat ≥100	0	
5. Limit consumption of sugar-sweetened drinks	**Total sugar-sweetened drinks (grams/day):**		Baseline or Endpoint nutritional assessments, including 24-hour recall, WCRF checklist and FFQ
	0	1	
	>0 – ≤250	0.5	
	>250	0	
6. Limit alcohol consumption	**Total ethanol (grams/day):**		Baseline or Endpoint nutritional assessments, including 24-hour recall, WCRF checklist and FFQ
	0	1	
	≤14 (1 drink) females	0.5	
	>14 (1 drink) females	0	
7. For mothers: breastfeed your baby, if you can	**Exclusively breastfed over lifetime for a total of:**		Baseline nutritional assessment, dietitian verbally collected response.
	6+ months	1	
	>0 – <6 months	0.5	
	Never	0	
		Total Score / 7	

Abbreviations: AICR, American Institute Cancer Research; BMI, Body Mass Index; FFQ, Food Frequency Questionnaire; WCRF, World Cancer Research Fund

CHAPTER 5 SUPPLEMENTARY MATERIAL

Supplementary Table 5.1: Coding use in Food Frequency Questionnaire Supplement Assessment

Supplementary Table 5.2: Frequency of Supplement Use by Participants at Baseline (n = 187)

Supplementary Table 5.3: Profile of Daily Supplement Users at Baseline and Endpoint

Supplementary Table 5.1: Coding use in Food Frequency Questionnaire Supplement Assessment

Variable	Numerical Code
Supplement Use	
Yes	1
No	2
Sometimes	3
Frequency of Use	
Never or less than once a month	1
1 to 3 times per month	2
Once a week	3
2 to 4 times per week	4
5 to 6 times per week	5
Once a day	6

Supplementary Table 5.2: Frequency of Supplement Use by Participants at Baseline (n = 187)

Supplement Type	Once a Day n (%)	5-6/week n (%)	2–4/week n (%)	Once a week n (%)	1–3 /month n (%)	Rarely/None n (%)
Vitamins & Minerals						
Vitamin D	31 (16.6)	5 (2.7)	16 (8.6)	6 (3.2)	12 (6.4)	5 (2.7)
Calcium + Vitamin D	27 (14.4)	5 (2.7)	24 (12.8)	4 (2.1)	8 (4.3)	1 (0.5)
Multivitamin	22 (11.8)	7 (3.7)	12 (6.4)	9 (4.8)	8 (4.3)	4 (2.1)
Vitamin C	6 (3.2)	4 (2.1)	5 (2.7)	6 (3.2)	5 (2.7)	1 (0.5)
Magnesium	5 (2.7)	1 (0.5)	6 (3.2)	3 (1.6)	0 (0.0)	1 (0.5)
Zinc	3 (1.6)	0 (0.0)	0 (0.0)	2 (1.1)	2 (1.1)	1 (0.5)
Iron	4 (2.1)	0 (0.0)	2 (1.1)	2 (1.1)	0 (0.0)	0 (0.0)
Other Vitamins*	≤2 (≤1.1)	—	—	—	—	—
Herbal & Botanical						
Evening Primrose Oil	11 (5.9)	2 (1.1)	2 (1.1)	2 (1.1)	1 (0.5)	0 (0.0)
Turmeric / Curcumin	3 (1.6)	0 (0.0)	3 (1.6)	1 (0.5)	0 (0.0)	0 (0.0)
Herbal Botanical Blend	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sage, Echinacea, Milk Thistle, Maca, Rhodiola, Spirulina, Seamoss, Andrographis, Quercetin	≤1 (≤0.5) each	—	—	—	—	—
Oils & Other Supplements						
Fish Oils	12 (6.4)	2 (1.1)	7 (3.7)	0 (0.0)	0 (0.0)	2 (1.1)
Flaxseed Oil	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Glucosamine Sulphate	4 (2.1)	0 (0.0)	1 (0.5)	0 (0.0)	2 (1.1)	0 (0.0)
Probiotic	7 (3.7)	1 (0.5)	2 (1.1)	1 (0.5)	6 (3.2)	3 (1.6)
Amino Acids	2 (1.1)	0 (0.0)	1 (0.5)	1 (0.5)	1 (0.5)	0 (0.0)
Brewer's Yeast, Guarana, Red Yeast Rice	≤1 (≤0.5) each	—	—	—	—	—

* Includes Vitamin A, B-complex, B12, B3, B6, B7, B9, K (all ≤1.6% daily use).

Supplementary Table 5.3: Profile of Daily Supplement Users at Baseline and Endpoint

Demographic	Baseline Daily Supplement Use n = 86	%	Demographic	Endpoint Daily Supplement Use n = 112	%
Age Group					
<40	3	3%	<40	8	7%
40-44	7	8%	40-44	9	8%
45-54	22	26%	45-54	32	29%
54-59	20	23%	54-59	25	22%
60-64	14	16%	60-64	14	13%
65-69	11	13%	65-69	13	12%
70+	9	10%	70+	11	10%
Menopause Status					
Post	56	65%	Post	66	59%
Pre	20	23%	Pre	31	28%
Peri	8	9%	Peri	12	11%
Unknown	2	2%	Unknown	3	3%
Cancer					
Breast	75	87%	Breast	96	86%
Cervical	3	3%	Cervical	8	7%
Endometrial	8	9%	Endometrial	8	7%
BMI Category					
<18.5	1	1%	<18.5	0	0%
18.5 - 24.9	30	35%	18.5 - 24.9	30	27%
25.0 - 29.9	23	27%	25.0 - 29.9	25	22%
30 - 34.9	17	20%	30 - 34.9	15	13%
> 35	15	17%	> 35	15	13%
Ethnicity					
Any other white background	7	8%	Any other white background	9	8%
White Irish	79	92%	White Irish	102	91%
			Chinese	1	1%
Education Level					
Third level (college/university)	55	64%	Third level (college/university)	77	69%
Secondary level	30	35%	Secondary level	34	30%
Primary level	1	1%	Primary level	1	1%

Martial Status					
Cohabiting	5	6%	Cohabiting	11	10%
Divorced	4	5%	Divorced	6	5%
Married	56	65%	Married	71	63%
Separated	4	5%	Separated	6	5%
Single	14	16%	Single	13	12%
Widowed	3	3%	Widowed	5	4%
Smoking					
No	83	97%	No	104	93%
Yes	3	3%	Yes	8	7%
Alcohol					
No	19	22%	No	28	25%
Yes	67	78%	Yes	84	75%
Economic Certainty					
Coping on present income	35	41%	Coping on present income	49	44%
Difficult on present income	8	9%	Difficult on present income	13	12%
Living comfortably on present income	39	45%	Living comfortably on present income	45	40%
Very difficult on present income	4	5%	Very difficult on present income	4	4%
Economic Status at Baseline					
Employed	27	31%	Employed	37	33%
Looking after home/family	10	12%	Looking after home/family	12	11%
Retired	18	21%	Other reasons	2	2%
Student	2	2%	Retired	20	18%
Unable to work due to COVID restrictions	1	1%	Student	3	3%
Unable to work due to sickness or disability	26	30%	Unable to work due to sickness or disability	32	29%
Unemployed, not looking for a job	2	2%	Unemployed, looking for a job	3	3%
			Unemployed, not looking for a job	3	3%
Baseline Supplement Use			**Endpoint Supplement Use**		
Sometimes	3	3%	Yes	112	100%
Yes	83	97%			
Baseline VMS Use			**Endpoint VMS Use**		

Yes	86	100%	No	2	2%
			Yes	110	98%
Baseline HBS Use			**Endpoint HBS Use**		
No	55	64%	No	75	67%
Yes	31	36%	Yes	37	33%
Baseline EORTC Score					
40 - 49	20	23%	40 - 49	42	38%
50 - 59	31	36%	50 - 59	40	36%
60 - 69	19	22%	60 - 69	16	14%
70 - 79	13	15%	70 - 79	9	8%
80 - 89	1	1%	80 - 89	4	4%
90 - 99	2	2%	90 - 99	1	1%
Fatigue					
A little bit	35	41%	A little bit	49	44%
Extremely	7	8%	Extremely	4	4%
Not at all	8	9%	Not at all	13	12%
Quite a bit	22	26%	Quite a bit	20	18%
Somewhat	14	16%	Somewhat	26	23%
Insomnia					
Mild	22	26%	Mild	39	35%
Moderate	31	36%	Moderate	39	35%
None	13	15%	None	22	20%
Severe	16	19%	Severe	8	7%
Very Severe	4	5%	Very severe	4	4%
Concentration					
Mild	28	33%	Mild	50	45%
Moderate	24	28%	Moderate	23	21%
None	22	26%	None	30	27%
Severe	9	10%	Severe	7	6%
Very Severe	3	3%	Very severe	2	2%
Memory					
Mild	36	42%	Mild	55	49%
Moderate	23	27%	Moderate	27	24%
None	18	21%	None	23	21%
Severe	5	6%	Severe	5	4%
Very Severe	4	5%	Very severe	2	2%

General Pain					
Mild	31	36%	Mild	33	29%
Moderate	28	33%	Moderate	35	31%
None	14	16%	None	24	21%
Severe	9	10%	Severe	19	17%
Very Severe	4	5%	Very severe	1	1%
Joint Pain					
Mild	27	31%	Mild	38	34%
Moderate	26	30%	Moderate	36	32%
None	16	19%	None	19	17%
Severe	14	16%	Severe	17	15%
Very Severe	3	3%	Very severe	2	2%
Abdominal Pain					
Mild	22	26%	Mild	30	27%
Moderate	13	15%	Moderate	11	10%
None	48	56%	None	70	63%
Severe	2	2%	Severe	1	1%
Very Severe	1	1%			
Hot Flash					
Mild	17	20%	Mild	21	19%
Moderate	31	36%	Moderate	36	32%
None	19	22%	None	28	25%
Severe	15	17%	Severe	23	21%
Very Severe	4	5%	Very severe	4	4%
Vaginal Dryness					
Mild	18	21%	Mild	38	34%
Moderate	16	19%	Moderate	22	20%
None	41	48%	None	37	33%
Severe	8	9%	Severe	10	9%
Very Severe	3	3%	Very severe	5	4%
Decreased Libido					
Mild	14	16%	Mild	26	23%
Moderate	15	17%	Moderate	29	26%
None	22	26%	None	26	23%
Severe	19	22%	Severe	14	13%
Very Severe	16	19%	Very severe	17	15%
Constipation					

Mild	16	19%	Mild	25	22%
Moderate	12	14%	Moderate	13	12%
None	48	56%	None	63	56%
Severe	7	8%	Severe	9	8%
Very Severe	3	3%	Very severe	2	2%
Fear of Recurrence Frequency					
Almost Constantly	4	5%	Almost constantly	4	4%
Frequently	16	19%	Frequently	11	10%
Never	11	13%	Never	22	20%
Occasionally	32	37%	Occasionally	54	48%
Rarely	23	27%	Rarely	21	19%
Weight Gain Concern					
No	27	31%	No	39	35%
Unsure	4	5%	Unsure	8	7%
Yes	55	64%	Yes	65	58%
Moderate to Vigorous Activity Per Week					
Between 75 to 150 minutes	29	34%	Between 75 minutes & less than 150 minutes	37	33%
Less than 75 minutes	35	41%	Less than 75 minutes	45	40%
More than 150 minutes	22	26%	More than 150 minutes	30	27%
Vigorous Activity Per Week					
Between 75 to 150 minutes	12	14%	Between 75 & less than 150 minutes	24	21%
Less than 75 minutes	69	80%	Less than 75 minutes)	76	68%
More than 150 minutes	5	6%	More than 150 minutes	12	11%

Abbreviations: BMI, Body Mass Index; EORTC, European Organisation for Research and Treatment of Cancer; HBS, Herbal Botanical Supplements; VMS, Vitamin and Mineral Supplements

CHAPTER 6 SUPPLEMENTARY MATERIAL

Supplementary File:	Clinical Research Ethics Committee of Cork University Teaching Hospitals
Supplementary Table 6.1:	Data Collection Instrument – Online Survey
Supplementary Table 6.2:	Use of Herbal Supplements for Symptom Relief (n = 75)
Supplementary Table 6.3:	Use of Vitamin and Mineral Supplements for Symptom Relief (n = 75)

Supplementary File: Clinical Research Ethics Committee of Cork University Teaching Hospitals Response

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Clinical Research Ethics Committee of the Cork Teaching Hospitals

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CREC Review Reference Number: ECM 4 (mm) 05/12/2023
& ECM 3 (ooooo) 11/03/2025

Date: 14th March 2025

Dr Samantha Cushen
Department of Food and Nutritional Sciences
University College Cork
College Road
Cork

Study Title: The use of Dietary and Herbal Supplements to Alleviate Menopausal Symptoms in Female Cancer Survivors.

Dear Dr Cushen

The following documents have been approved:

Document	Approved	Version	Date
Amendment Application Form	Yes		Signed: 27th February 2025
Protocol Amendment Application and Supplementary Information Report Form	Yes		Signed: 3rd March 2025
Study Protocol	Yes	3	February 2025
Participant Information Leaflet/Informed Consent Form (Combined)	Yes	3	February 2025
Data Collection Instrument – web-based survey	Yes	2	February 2025
Online Survey Poster	Yes	4	

Approval is granted to implement this amendment.

Yours sincerely

Professor Brendan Buckley
Interim Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

Supplementary Table 6.1: Data Collection Instrument – Online Survey

1. **What is your gender?**
   - □ Female
   - □ Male
   - □ Non-Binary
   - □ Gender Fluid
   - □ Transgender
   - □ Intersex
   - □ Other

Please describe other

2. **What sex were you assigned at birth?**
   - □ Female
   - □ Male

If "Male" is selected in QUESTION 2, please stop the survey and display the following verbiage:

"Thank you for your interest in this University College Cork study. To learn more about our studies, please visit XXXXX."

3. Which of the following age ranges do you fit into?

- □ 18-24
- □ 25-29
- □ 30-39
- □ 40-49
- □ 50-59
- □ 60-69
- □ 70+

4. What county do you live in?

- □ Antrim
- □ Armagh
- □ Carlow

□ Cavan

□ Clare

□ Cork

□ Derry

□ Donegal

□ Down

□ Dublin

□ Fermanagh

□ Galway

□ Kerry

□ Kildare

□ Kilkenny

□ Laois

□ Leitrim

□ Limerick

□ Longford

□ Louth

□ Mayo

□ Meath

□ Monaghan

□ Offaly

□ Roscommon

□ Sligo

□ Tipperary

□ Tyrone

□ Waterford

□ Westmeath

□ Wexford

□ Wicklow

5. Are you in paid employment?

□ Yes

□ No

6. How many hours a week do you currently work?

□ 0 – 8 hours

□ 8 – 16 hours

□ 16 – 24 hours

□ 24 – 32 hours

□ 32 – 40 hours

□ 40 + hours

7. What is your highest level of education?

□ No formal education

□ Primary education

□ Second level education (Junior Certificate, Leaving Certification, Technical or Vocational Qualification)

□ Third level education (Bachelor's Degree, Postgraduate Certificate or Diploma)

□ Third level education (Postgraduate Degree)

□ Doctorate (Ph.D)

8. Have you been diagnosed with cancer?

□ Yes

□ No

If "No" is selected in QUESTION 8, please stop the survey and display the following verbiage:

"Thank you for your interest in this University College Cork study. To learn more about our studies, please visit ucc.ie."

9. Please select the type of primary cancer you have been diagnosed with:

□ Bladder

□ Brain and Spinal Cord

□ Breast

□ Cancer of Unknown Primary

□ Colorectal

□ Endometrial

□ Hodgkin Lymphoma

□ Leukaemia

□ Liver

□ Multiple Myeloma

□ Non-Hodgkin Lymphoma

□ Oesophageal

□ Ovarian

□ Pancreatic

□ Renal

□ Skin

□ Stomach

□ Thyroid

□ Other

10. Is the cancer you have been diagnosed with curative or metastatic (spread to other parts of the body)?

□ Curative

□ Metastatic

□ Unsure

11. How many years ago were you first diagnosed with cancer?

□ Less than 1 year ago

□ 1 – 2 years ago

□ 3 – 5 years ago

□ 5 – 10 years ago

□ More than 10 years ago

12. What treatments have you received to date? Tick all boxes that apply.

□ Chemotherapy
□ Immunotherapy (such as Herceptin, used to treat certain types of breast cancer and stomach cancer)
□ Radiotherapy - including external beam radiotherapy and internal radiotherapy (brachytherapy)
□ Surgery (such as a lumpectomy, hysterectomy or mastectomy)
□ Endocrine or hormone blocking therapy (like anastrozole or tamoxifen)
□ Other

Please describe other

13. What treatments (if any) are you currently undergoing? (Tick all that apply)

□ Chemotherapy
□ Immunotherapy (such as Herceptin, used to treat certain types of breast cancer and stomach cancer)
□ Radiotherapy - including external beam radiotherapy and internal radiotherapy (brachytherapy)

□ Surgery: Planned

□ Surgery: Completed

□ Endocrine / Hormone Blocking Therapy (like anastrozole or tamoxifen)

□ On a break from treatment

□ Finished treatment (in remission)

□ Other

Please describe other

14. Have you ever been prescribed an endocrine therapy?

Endocrine therapy is often prescribed for certain types of breast cancer. It works by blocking oestrogen in certain parts of the body. It is usually a tablet, and you take one every day.

□ Yes (if yes, question 15 will appear)
□ No (if no, question 16 will appear)

15. What endocrine therapy are you currently prescribed?

□ Tamoxifen
□ Anastrozole (Arimidex)
□ Letrozole (Femora)
□ Exemestane (Aromasin)
□ I'm prescribed an endocrine therapy but I am not sure which one.

16. Which stage of menopause would you describe yourself as being in currently?

□ Pre-Menopausal (this is where you have no symptoms of perimenopause or menopause. You still have a period.)
□ Peri-Menopausal (this is the transitional period before the menopause.)

□ Post-Menopausal (the time after menopause, when a you have not had a period for over a year.)
□ I'm having menopausal symptoms, but I'm not sure what stage of the menopause I am in.
□ I have no menopausal symptoms and I am unsure of what stage I am in.

If "Pre-Menopause" is selected in QUESTION 16, display the following verbiage:

"Thank you for participating in our study. Your time and effort is appreciated. The information you provided will help women who are currently transitioning through menopause, and we hope that you can benefit from our survey findings in the future."

If "Peri-Menopausal" OR "Post-Menopausal" is selected in QUESTION 16, proceed to QUESTION 17:

17. Please rate your experience of symptoms which have sometimes been associated with menopause. Consider your experience with these symptoms *over the last 1 month*.

	NOT AT ALL	MILD	MODERATE	SEVERE
Hot flashes	○	○	○	○
Insomnia (trouble sleeping)	○	○	○	○
Tingling/prickling sensation (or pain) in extremities (arms and/or legs)	○	○	○	○
Dizziness	○	○	○	○
Depression	○	○	○	○
Fatigue	○	○	○	○
Extreme Tiredness	○	○	○	○
Muscle aches	○	○	○	○
Headaches	○	○	○	○
Heart palpitations (racing heart, irregular beats)	○	○	○	○
Nervousness	○	○	○	○
Night sweats	○	○	○	○
Irritability (mood swings)	○	○	○	○
Vaginal dryness	○	○	○	○
Skin dryness or changes	○	○	○	○
Hair loss	○	○	○	○
Lack of focus (easily physically or mentally exhausted, poor concentration)	○	○	○	○
Poor memory (forgetfulness)	○	○	○	○
Low sex drive	○	○	○	○
Other _____	○	○	○	○
Other _____	○	○	○	○

18. Are your menopausal symptoms treatment-induced? This can occur due to chemotherapy, anti-cancer medications, ovary removal surgery or radiotherapy.

□ Yes

□ No

□ Not sure

19. Are you currently taking Hormone Replacement Therapy (HRT) (e.g. Oestrogen or combined HRT tablets, oestrogen or combined HRT patch, progesterone- mirena coil, oestrogen or combined HRT cream or spray or testosterone)?

□ Yes

□ No

EXPLANATION PAGE OF NEXT SECTION:

In the next section, we will be asking you questions about any vitamins and minerals or herbal and botanical supplements, that you might be taking.

When we refer to herbal or botanical remedies, we are discussing supplements such as sage and evening primrose oil, melatonin, green tea etc. When we refer to vitamins and minerals, we are discussing vitamin supplements like Vitamin D, and mineral supplements like Calcium and Magnesium

Whilst we have suggested herbal or botanical remedies for the purpose of this research, we cannot recommend their safety or efficacy.

20. Do you currently take any Herbal / Botanical Remedies for menopausal symptoms?

□ Yes

□ No

□ Unsure

If "No" is selected in QUESTION 20, <u>do not</u> display QUESTION 21 and proceed to QUESTION 25:

If "Yes" or "Unsure" is selected in QUESTION 20, proceed to QUESTION 21.

21. What herbal remedies have you ever used to combat your menopausal symptoms? Please check all that apply.

- Ashwagandha
- Asian Mushrooms (e.g Lion's Mane)
- Black Cohosh
- Collagen
- Echinacea
- Evening Primrose Oil
- Ginseng

- Maca Root
- Melatonin
- Milk Thistle
- Quercetin
- Red Clover
- Red Yeast Rice
- Rose Hip Oil
- Sage
- Slippery Elm Bark
- Soy Isoflavones (sometimes called phytoestrogens)
- Tart Cherry
- Turmeric or Curcumin
- I have not tried any of these
- Other

Please describe other

22. **Please indicate <u>why</u> you are taking these herbal remedies or for what menopausal symptoms**

Please display only those remedies in QUESTION 22 that are <u>checked</u> in QUESTION 21:

	Symptom I take herbal remedy for
Ashwagandha	
Asian Mushrooms (e.g Lion's Mane)	
Black Cohosh	
Collagen	
Echinacea	
Evening Primrose Oil	
Ginseng	
Maca Root	
Melatonin	
Milk Thistle	
Quercetin	
Red Clover	
Red Yeast Rice	
Rose Hip Oil	
Sage	
Slippery Elm Bark	
Soy Isoflavones (sometimes called phytoestrogens)	
Tart Cherry	
Turmeric or Curcumin	
Other	

23. Please rate how effective these remedies were at reducing your menopausal symptoms.

Please display only those remedies in QUESTION 23 that are <u>checked</u> in QUESTION 21:

	NOT AT ALL	***SOMEWHAT***	***VERY***
Ashwagandha	○	○	○
Asian Mushrooms (e.g Lion's Mane)	○	○	○
Black Cohosh	○	○	○
Collagen	○	○	○
Echinacea	○	○	○
Evening Primrose Oil	○	○	○
Ginseng	○	○	○
Maca Root	○	○	○
Melatonin	○	○	○
Milk Thistle	○	○	○
Quercetin	○	○	○
Red Clover	○	○	○
Red Yeast Rice	○	○	○
Rose Hip Oil	○	○	○
Sage	○	○	○
Slippery Elm Bark	○	○	○
Soy Isoflavones (sometimes called phytoestrogens)	○	○	○
Tart Cherry	○	○	○
Turmeric or Curcumin	○	○	○
Other	○	○	○

24. Please indicate the primary source of information when choosing to take a herbal remedy

Please display only those remedies in QUESTION 24 that are <u>checked</u> in QUESTION 21:

	CORU/HCPC Registered Dietitian	***Primary Consultant/ General Practitioner (GP)***	***Other healthcare professional (nurse, pharmacist)***	***Family and/or friends***	***Other female cancer survivors***	***Internet or Social Media***	***Health store assistant***	***Nutritional Therapist or Nutritional Coach***
Ashwagandha	○	○	○	○	○	○	○	○
Asian Mushrooms	○	○	○	○	○	○	○	○

(e.g Lion's Mane)								
Black Cohosh	○	○	○	○	○	○	○	○
Collagen	○	○	○	○	○	○	○	○
Echinacea	○	○	○	○	○	○	○	○
Evening Primrose Oil	○	○	○	○	○	○	○	○
Ginseng	○	○	○	○	○	○	○	○
Maca Root	○	○	○	○	○	○	○	○
Melatonin	○	○	○	○	○	○	○	○
Milk Thistle	○	○	○	○	○	○	○	○
Quercetin	○	○	○	○	○	○	○	○
Red Clover	○	○	○	○	○	○	○	○
Red Yeast Rice	○	○	○	○	○	○	○	○
Rose Hip Oil	○	○	○	○	○	○	○	○
Sage	○	○	○	○	○	○	○	○
Slippery Elm Bark	○	○	○	○	○	○	○	○
Soy Isoflavones (sometimes called phytoestrogens)	○	○	○	○	○	○	○	○
Tart Cherry	○	○	○	○	○	○	○	○
Turmeric or Curcumin	○	○	○	○	○	○	○	○
Other	○	○	○	○	○	○	○	○

25. Do you currently take any Vitamin / Mineral Supplement for menopausal symptoms?

□ Yes

□ No

□ Unsure

If "No" is selected in QUESTION 25, <u>do not</u> display QUESTION 26 and proceed to QUESTION 30:

If "Yes" or "Unsure" is selected in QUESTION 25, proceed to QUESTION 26.

26. What vitamin/ mineral supplement have you ever used to combat your menopausal symptoms? Please check all that apply.

- o Amino Acid (such as L-Lysine)
- o Calcium
- o Fish oil – such as cod liver oil or fish oil blend
- o Glucosamine
- o Iron
- o Magnesium
- o Multivitamin *
- o Menopause Specific Multivitamin *
- o Omega 3 fish oil (containing EPA & DHA)
- o Probiotic
- o Selenium
- o Vitamin A
- o Vitamin B complex
- o Vitamin B1
- o Vitamin B12
- o Vitamin B3
- o Vitamin B6
- o Vitamin B7
- o Vitamin B9
- o Vitamin C
- o Vitamin D
- o Vitamin E
- o Vitamin K
- o Zinc
- o I have not tried any of these
- o Other
- o

*If multivitamin checked, please define the brand of multivitamin you use.

*If menopause-specific multivitamin checked, please define the brand of you use.

Please describe other

27. **Please indicate <u>why</u> you are taking these vitamin/mineral supplements or for what menopausal symptoms**

Please display only those remedies in QUESTION 26 that are <u>checked</u> in QUESTION 25:

	Symptom I take vitamin/mineral supplement for
Amino Acid (such as L-Lysine)	
Calcium	

Fish oil – such as cod liver oil or fish oil blend
Glucosamine
Iron
Magnesium
Multivitamin *
Omega 3 fish oil (containing EPA & DHA only)
Probiotic
Selenium
Vitamin A
Vitamin B complex
Vitamin B1
Vitamin B12
Vitamin B3
Vitamin B6
Vitamin B7
Vitamin B9
Vitamin C
Vitamin D
Vitamin E
Vitamin K
Zinc
I have not tried any of these
Other

28. Please rate how effective these vitamin and mineral supplements were at reducing your menopausal symptoms.

Please display only those remedies in QUESTION 28 that are <u>checked</u> in QUESTION 26:

	NOT AT ALL	***SOMEWHAT***	***VERY***
Amino Acid (such as L-Lysine)	○	○	○
Calcium	○	○	○
Fish oil – such as cod liver oil or fish oil blend	○	○	○
Glucosamine	○	○	○
Iron	○	○	○
Magnesium	○	○	○
Multivitamin *	○	○	○
Omega 3 fish oil (containing EPA & DHA only)	○	○	○
Probiotic	○	○	○
Selenium	○	○	○
Vitamin A	○	○	○
Vitamin B complex	○	○	○

Vitamin B1	○	○	○
Vitamin B12	○	○	○
Vitamin B3	○	○	○
Vitamin B6	○	○	○
Vitamin B7	○	○	○
Vitamin B9	○	○	○
Vitamin C	○	○	○
Vitamin D	○	○	○
Vitamin E	○	○	○
Vitamin K	○	○	○
Zinc	○	○	○
I have not tried any of these	○	○	○
Other	○	○	○

29. Please indicate the primary source of information when choosing to take a vitamin or mineral supplement

Please display only those remedies in QUESTION 29 that are <u>checked</u> in QUESTION 26:

	CORU/HCPC Registered Dietitian	*Primary Consultant/ General Practitioner (GP)*	*Other healthcare professional (nurse, pharmacist)*	*Family and/or friends*	*Other female cancer survivors*	*Internet or Social Media*	*Health store assistant*	*Nutritional Therapist or Nutritional Coach*
Amino Acid (such as L-Lysine)	○	○	○	○	○	○	○	○
Calcium	○	○	○	○	○	○	○	○
Fish oil – such as cod liver oil or fish oil blend	○	○	○	○	○	○	○	○
Glucosamine	○	○	○	○	○	○	○	○
Iron	○	○	○	○	○	○	○	○
Magnesium	○	○	○	○	○	○	○	○
Multivitamin *	○	○	○	○	○	○	○	○
Omega 3 fish oil (containing EPA & DHA only)	○	○	○	○	○	○	○	○
Probiotic	○	○	○	○	○	○	○	○
Selenium	○	○	○	○	○	○	○	○
Vitamin A	○	○	○	○	○	○	○	○
Vitamin B complex	○	○	○	○	○	○	○	○

Vitamin B1	○	○	○	○	○	○	○	○
Vitamin B12	○	○	○	○	○	○	○	○
Vitamin B3	○	○	○	○	○	○	○	○
Vitamin B6	○	○	○	○	○	○	○	○
Vitamin B7	○	○	○	○	○	○	○	○
Vitamin B9	○	○	○	○	○	○	○	○
Vitamin C	○	○	○	○	○	○	○	○
Vitamin D	○	○	○	○	○	○	○	○
Vitamin E	○	○	○	○	○	○	○	○
Vitamin K	○	○	○	○	○	○	○	○
Zinc	○	○	○	○	○	○	○	○
Other	○	○	○	○	○	○	○	○

30. Have you discussed any of the vitamin/mineral or herbal/botanical supplements with your medical team?

□ Yes

□ No

□ Not applicable

31. Would you like to give a reason as to why you have or have not discussed this with your medical team?

□ Yes – I have discussed this with my medical team.

□ Yes – I have not discussed this with my medical team.

□ No

□ Not applicable

If "No" is selected in QUESTION 31, <u>do not</u> display QUESTION 31.1 and proceed to QUESTION 32:

If yes is selected in QUESTION 31, proceed to QUESTION 31.1.

31.1 Please use the box below to discuss to explain why you have decided to discuss your supplements with your medical team:

31.1 Please use the box below to discuss to explain why you have decided not to discuss your supplements with your medical team:

32. Are you taking any additional supplements we did not mention. ***(OPTIONAL)***

BLANK COMMENT BOX

ANSWER NOT REQUIRED FOR SURVEY COMPLETION

Thank you for your contribution to this research. Your time is extremely valued.

For information on how to manage menopausal symptoms following a cancer diagnosis, please use this link to a five-part webinar series “Menopause, Diet and Cancer”: https://youtu.be/rs6DX3GWxYU?si=qB42wlkQfqHNjjoC&t=7

As always, please consult your medical team or a registered dietitian specialising in oncology for individualised recommendations.

Supplementary Table 6.2: Use of Herbal Supplements for Symptom Relief (n = 75)

Patient Reported Symptoms Indicated for Herbal Supplement Use	N	%
Ashwagandha		
Anxiety	3	*4%*
Sleep	2	*3%*
Stress	1	*1%*
Asian Mushrooms (e.g. Lion's Mane)		
Cognitive symptoms	4	*5%*
Digestive symptoms	1	*1%*
Immunity	2	*3%*
Irritability	2	*3%*
Night Sweats	1	*1%*
Overall Menopause Symptoms	2	*3%*
Collagen		
Hair Thinning	1	*1%*
Joint Pain	3	*4%*
Skin	3	*4%*
Echinacea		
Immunity	1	*1%*
Evening Primrose Oil		
Hot Flushes and Night Sweats	3	*4%*
General Health	1	*1%*
Joint Aches	1	*1%*
Pain	1	*1%*
Tamoxifen Side Effects	1	*1%*
Ginseng		
Energy	1	*1%*
Decreased Libido	1	*1%*
Melatonin		
Fatigue	1	*1%*
Insomnia	8	*11%*
Immunity	1	*1%*
Red Clover		
Hormonal Balance	1	*1%*
Red Yeast Rice		
Cholesterol	1	*1%*
Rose Hip Oil		
Dry Skin	1	*1%*
Sage		
Cognitive symptoms	1	*1%*
Hot Flashes	3	*4%*
Slippery Elm Bark		

Digestive symptoms	1	*1%*
Tart Cherry		
Bone Pain	2	*3%*
Fatigue	1	*1%*
Insomnia	1	*1%*
Joint Pain	1	*1%*
Turmeric and/or Curcumin		
Inflammation	5	*7%*
Immunity	1	*1%*
Joint Pain	1	*1%*
Pain	1	*1%*

Supplementary Table 6.3: Use of Vitamin and Mineral Supplements for Symptom Relief (n = 75)

Patient Reported Symptoms Indicated for Vitamin and Mineral Supplement Use	**N**	**%**
Calcium		
Bone Health	29	*38.7%*
Fish Oil - such as cod liver oil or fish oil blend		
Bone health	1	*1.3%*
Cognitive symptoms	4	*5.3%*
Dietary supplement	1	*1.3%*
General Health	2	*2.7%*
Heart Health	1	*1.3%*
Hot Flushes	1	*1.3%*
Joint Pain	2	*2.7%*
Glucosamine		
Joint Pain	5	*6.7%*
Iron		
Anaemia	1	*1.3%*
Bones	1	*1.3%*
Chemotherapy side effects	1	*1.3%*
Energy	1	*1.3%*
Fatigue	1	*1.3%*
General Health	1	*1.3%*
Hair Loss	1	*1.3%*
Joint Pain	1	*1.3%*
Magnesium		
Bone Health	5	*6.7%*
Cramps	5	*6.7%*
Fatigue	1	*1.3%*
Heart Health	1	*1.3%*
Insomnia	23	*30.7%*
Joint Pain	5	*6.7%*
Muscle Pain	6	*8.0%*
Menopause Specific-Multivitamin		
Overall Menopause Symptoms	4	*5.3%*
Multivitamin		
Bone Health	1	*1.3%*
Energy	4	*5.3%*
Fatigue	1	*1.3%*
General Health	4	*5.3%*
Immunity	3	*4.0%*
Insomnia	1	*1.3%*
Omega 3 Fish Oil (containing EPA & DHA only)		

Anti-inflammatory	1	*1.3%*
Bone Health	1	*1.3%*
Cognitive symptoms	10	*13.3%*
Heart Health	3	*4.0%*
Dietary supplement	2	*2.7%*
Gut Health	1	*1.3%*
Joint Pain	5	*6.7%*
Probiotic (such as a sachet or capsule)		
Gut Health	5	*6.7%*
Gastrointestinal Symptoms	2	*2.7%*
General Health	1	*1.3%*
Immunity	2	*2.7%*
Skin	1	*1.3%*
Thrush	1	*1.3%*
Selenium		
General Health	2	*2.7%*
Vitamin A		
General Health	2	*2.7%*
B Vitamins		
General Health	6	*8.0%*
Hair, Skin and Nails	2	*2.7%*
B12 Deficiency	1	*1.3%*
Cognitive symptoms	3	*4.0%*
Vitamin C		
Bone Health	2	*2.7%*
General Health	3	*4.0%*
Immunity	5	*6.7%*
Vitamin E		
Anti-Inflammatory	1	*1.3%*
General Health	2	*2.7%*
Vitamin D		
Bone Health	28	*37.3%*
Cognitive symptoms	5	*6.7%*
Immunity	3	*4.0%*
Muscles	1	*1.3%*
General Health	4	*5.3%*
Vitamin K		
Absorption of Vitamin D	2	*2.7%*
Bone Health	1	*1.3%*
General Health	1	*1.3%*
Heart Health	1	*1.3%*
Zinc		
General Health	4	*5.3%*
Immunity	3	*4.0%*
Thyroid	1	*1.3%*

CHAPTER 7 SUPPLEMENTARY MATERIAL

Supplementary Table 7.1: Recipe Collection Adherence to Elements of the Mediterranean Diet Principles

Supplementary Table 7.2: Overview of Webinar Series Content

Supplementary Table 7.1: Recipe Collection Adherence to Elements of the Mediterranean Diet Principles

Recipe (values per serving)	Wholegrain Carbohydrates	Fruit and Vegetables	Pulses and Legumes	Poultry and Fish	Dairy Products
Breakfast					
Tahini and Cardamom Granola	<0.5 serving	0 servings	<0.5 serving	0 servings	0 servings
Shakshuka: Family Style	0 servings	1.5 servings	0 servings	0 servings	0.5 servings
Overnight Oats					
Tropical	1 serving	1.5 servings	0 servings	0 servings	> 0.5 – 1 serving
Raspberry and Dark Chocolate	1 serving	1 serving	0 servings	0 servings	> 0.5 – 1 serving
Nut Butter and Wild Blueberries	1 serving	0.5 serving	0.5 servings	0 servings	> 0.5 – 1 serving
Light Meals					
Brunch 4 Ways					
New York Style	1 serving	<0.5 serving	0 servings	> 0.5 – 1 serving	1 serving
Korean Style	1 serving	> 0.5 – 1 serving	<0.5 serving	0 servings	0 servings
Melbourne Style	1 serving	1 serving	0 servings	1 serving	0 servings
Mexican Style	1 serving	1.5 servings	> 0.5 – 1 serving	0 servings	0.5 serving
Elotes Corn Salad with Chicken	0 servings	3.5 servings	0 servings	1 serving	<0.5 serving
Caprese Butter Bean Salad	0 servings	2 servings	1 serving	0 servings	1.5 servings
Main Meals					
Moroccan Chickpea Stew with Crispy Tofu	0 servings	4 servings	2 servings	0 servings	0 servings
Loaded Beef Burrito	1.5 servings	2 servings	1 serving	0 servings	<0.5 serving
One Pan Spanish Salmon and Rice	0.5 serving	3 servings	0 servings	1 serving	0 servings

Snacks					
Creamy Hummus	0 servings	<0.5 serving	<0.5 serving	0 servings	0 servings
Chocolate Trail Mix	0 servings	<0.5 serving	<0.5 serving	0 servings	0 servings
Kate's Kitchen Peanut Butter Balls	<0.5 serving	0 servings	<0.5 serving	0 servings	0 servings
Brain Bites	<0.5 serving	<0.5 serving	<0.5 serving	0 servings	<0.5 serving
Crackers: 4 Ways					
New York Style	1 serving	<0.5 serving	0 servings	0 servings	1 serving
Italian Style	1 serving	<1 serving	0 servings	0 servings	<1 serving
Moroccan Style	1 serving	0 servings	0.5 serving	0 servings	0 servings
English Style	1 serving	0.5 serving	0 servings	0 servings	1 serving
Desserts					
Carrot Cake with Tahini Cream Cheese	0 servings	<0.5 serving	0 servings	<0.5 serving	0.7 serving
Chocolate and Raspberry Traybake	0 servings	> 0.5 – 1 serving	0 servings	0 servings	<0.5 serving
The Everyday Dessert					
Summer Berry	0 servings	> 0.5 – 1 serving	0 servings	0 servings	1 serving
Apple Crisp	<0.5 serving	> 0.5 – 1 serving	0 servings	0 servings	1 serving
Peaches and Cream	0 servings	1 serving	0 servings	0 servings	1 serving
Chocolate and Strawberries	0 servings	> 0.5 – 1 serving	0 servings	0 servings	1 serving

Supplementary Table 7.2: Overview of Webinar Series Content

Webinar	Title	Learning Objectives	Content Outline	Time Allocated
General Introduction *Pre-Recorded*	Introduction	To understand what the webinar series is, its target audience and how to access the recordings and live webinar	• Introduction of hosts • Reasons for the webinar • Format of webinars • How and when to access and register for webinars	~ 5 minutes
1 *Pre-Recorded*	Body Composition and Bone Health	To understand the changes that can occur to your body during menopause; the importance of muscle mass and how to maintain it; the role of fat mass and heart health; the importance of bone health, calcium sources (including plant-based); and supplements commonly used.	Introduction: • Overview of the session Why do body composition changes occur? • Cancer treatment • Adjuvant endocrine therapies • Role of oestrogen and menopause • What can I expect might happen? Muscle mass: why is it important? • Impact of muscle, importance of muscle • How to fuel your muscles: protein sources • Exercise Fat Mass and Heart Health • Risk Awareness • Eating for heart health • Reading the labels, choosing the right fats Bone Health: • Osteoporosis risk • Endocrine therapy and menopause • Calcium sources and plant-based	~ 30 – 40 minutes

			Supplements • Common supplements, what to look for	
2 *Pre-Recorded*	Hot Flashes and Vasomotor Symptoms	To understand what vasomotor symptoms are and why they occur; the role of diet in managing vasomotor symptoms; and supplements commonly used	Introduction • Overview of the session What are vasomotor symptoms? • Mechanism behind vasomotor symptoms • Impact of endocrine therapy/cancer treatment on vasomotor symptoms The Role of Diet: • The Mediterranean Diet • Soya and Phyto-oestrogen after a hormone-receptor positive cancer diagnosis • Caffeine and Alcohol Supplements: • Common supplements, what to look for	~ 25 – 30 minutes
3 *Pre-Recorded*	Genitourinary Syndrome of the Menopause and Gut Health	To understand what genitourinary syndrome of the menopause is and why is occurs; eating well to manage genitourinary syndrome; why gut health is important and how to eat well to support it; and what supplements are commonly used.	Introduction • Overview of the session What is Genitourinary Syndrome of the Menopause • Why does it occur • Impact of cancer treatment and endocrine therapy The Role of Diet: • Prebiotics, Probiotics and Synbiotics • Low in Saturated Fat and Sugar • Drinking for a Healthy Bladder • Examples of a hydration for a healthy bladder	~ 30 minutes

			Gut Health: • Why is gut health important? • Pelvic Radiation Disease The Role of Diet: • Fibre – how much do we need, the benefits • Sources of fibre • Hydration • Prebiotics, probiotics Supplements • Common supplements, what to look for	
4 *Pre-Recorded*	Brain Health and Cognitive Function	To understand what psychological symptoms are and why they occur; the role of diet for brain health; and what supplements are commonly used.	Introduction • Overview of the session What are psychological symptoms? • Brain fog, irritability, anxiety, low mood, loss of confidence, mood swings • Why do they occur? The role of diet • Eating Patterns • Carbohydrates • Unsaturated fats • B Vitamins and Iron • Hydration and Caffeine • Alcohol Supplements: • Food first, supplement after • What to look our for • Common symptoms	~ 30 – 35 minutes

			Planning Ahead: • Meal Planning Template • Food Shopping Template	
5 *Live*	Menopause, Diet and Cancer: Live Q&A	To understand how to implement the information from Webinar 1 – 4 into practical everyday advice; body neutrality; strategies to eat well; dealing with misinformation; where to seek reliable support; and to engage with dietitians for a Q&A session	The LYSA Trial and Launch of *Menopause, Diet and Cancer* The Menopause Plate • The importance of the overall diet • How to ensure every meal is balanced Body Neutrality • Strategies to cope with changes that occur during menopause • Eating for health gain, not weight loss Strategies to Eat Well • Set the scene – recovering from treatment, back to work, perhaps looking after children • Meal Planning • Snack Planning • Shopping Lists Dealing with Misinformation • Supplements • Influencers • Social Media • "Quick Fixes" Where to Seek Support • Reliable sources of information Q&A Session (chaired by ICS)	~ 60 minutes