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THE NATIONAL UNIVERSITY OF IRELAND

UNIVERSITY COLLEGE CORK

SCHOOL OF FOOD AND NUTRITIONAL SCIENCES

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UCC

University College Cork, Ireland

Coláiste na hOllscoile Corcaigh

Vitamin K in the diet of the Irish population (1-90 years)

Thesis presented by:

Ciara Kingston, B.Sc.

For the degree of

DOCTOR OF PHILOSOPHY

(Nutritional Sciences)

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This thesis is dedicated to my wonderful parents who have supported myself and my brothers through all of life's endeavours.

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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

Ciara Kingston

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Personal Contribution to this thesis

This thesis is based on data from five national dietary surveys carried out by the Irish Universities Nutrition Alliance (www.iuna.net) over the last 20 years. These surveys included the National Children's Food Survey (5-12y) (2003-04), the National Teens' Food Survey (13-17y) (2005-06), the National Adult Nutrition Survey (18-90y) (2008-10), the National Pre-school Nutrition Survey (1-4y) (2010-11) and the National Children's Food Survey II (5-12y) (2017-18).

During this PhD, I worked with the Dietary Surveys Research Group in UCC. I was primarily responsible for assigning vitamin K_1 and vitamin K_2 composition values to all foods and beverages consumed by the Irish population collected through 5 national dietary surveys. I was also involved in the National Children's Food Survey II (NCFS II), carried out between April 2017 and May 2018 by the nutrition units in University College Cork, Cork Institute of Technology, University College Dublin and Technological University of Dublin. In my role as a fieldworker on this survey, I collected data from 50 participants including data related to dietary intake, health & lifestyle, eating behaviour, anthropometry in addition to the collecting and processing of spot urine samples from participants. I was also involved in data entry including entering of dietary intake data into Nutritics and the questionnaire data into DaSurvey. I was also involved in the development of the packaging database and in the quality control of the data collected throughout the survey.

All analyses in this thesis were performed by me. The attached work is entirely my own original work.

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Ciara Kingston

Publications

Conference abstracts

Kingston, C., Kehoe, L., McNulty, B. A., Nugent, A. P., Cashman, K. D., Flynn, A. & Walton, J. (2020). Updating of the Irish Food Composition Database for vitamin K1 and vitamin K2. *Proceedings of the Nutrition Society,* 79**,** E24.

Kingston, C., Kehoe, L., McNulty, B. A., Nugent, A. P., Cashman, K. D., Walton, J. & Flynn, A. (2019). Intakes and sources of menaquinones (vitamin K2) in the Irish population aged 1-90 years.13th European Nutrition Conference, FENS

Kingston, C., Kehoe, L., McNulty, B. A., Nugent, A. P., Cashman, K. D., Walton, J. & Flynn, A. (2018). Intakes and sources of vitamin K1 in Irish teenagers aged 13–17 years. *Proceedings of the Nutrition Society,* 77**,** E77.

Kingston, C., Kehoe, L., Walton, J., McNulty, B. A., Nugent, A. P., Cashman, K. D. & Flynn, A. (2017). Intakes and sources of Vitamin K1 in Irish pre-school children aged 1–4 years. *Proceedings of the Nutrition Society,* 76**,** E52.

Summary reports

Irish Universities Nutrition Alliance (2019) *National Children's Food Survey II: Summary report on Food and Nutrient Intakes, Body Weight, Physical Activity and Eating Behaviors in Children Aged 5-12 Years in Ireland* (contributing author)

Training/contributions during this training period

2017 PG6001: STEPS Scientific Training for Enhance Post Graduate Studies

2018 FE6600: An Introduction to the National & Global Food Sector

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2017-2019: PhD Student Representative on the Academic Committee in the School of Food and Nutritional Sciences, UCC

2019 Graduate of the **'Odyssey Programme'** (2019) in UCC which is designed to aid academic researchers expand their existing expertise to prepare for careers in industry

Abbreviations

Adequate Intake (AI)

Cork Institute of Technology (CIT)

Dietary Reference Value (DRV)

Estimated Average Requirement (EAR)

European Food Information Resource (EuroFIR)

European Food Safety Authority (EFSA)

European Prospective Investigation into Cancer and Nutrition (EPIC)

Irish Food Composition Database (IFCD)

Irish Universities Nutrition Alliance (IUNA)

Mean Daily Intake (MDI)

Meanaquinone-4 (MK-4)

Menaquinone-4-10 (MK-4-10)

Menaquinone-5-10 (MK-5-10)

National Adult Nutrition Survey (NANS)

National Children's Food Survey (NCFS)

National Children's Food Survey II (NCFS II)

National Diet and Nutrition Survey (NDNS)

National Health and Nutrition Examination Survey (NHANES)

National Pre-school Nutrition Survey (NPNS)

National Survey of Health and Development (NSHD)

National Teens' Food Survey (NTFS)

Nordic Council of Ministers (NCM)

North South Ireland Food Consumption Survey (NSIFCS)

Reference Nutrient Intake (RNI)

Technological University of Dublin (TUD)

UK Composition of Foods Integrated Dataset (COFID)

UK Department of Health (DoH)

Ratio of undercarboxylated osteocalcin to carboxylated osteocalcin (UCR)

United Stated Department of Agriculture (USDA)

University College Cork (UCC)

University College Dublin (UCD)

US Institute of Medicine (IOM)

Vitamin K Dependent (VKD)

World Health Organisation (WHO)

Abstract

Background: The role of vitamin K in maintaining normal blood coagulation is well established, however on-going research has suggested that vitamin K may have other roles in areas such as bone health, cardiovascular health, cognitive function and anti-inflammatory function. There are currently few data available on vitamin K intakes in nationally representative samples of population groups (partly due to limited composition data for vitamin K and its individual components) and the European Food Safety Authority (EFSA) have recently outlined the need for further data on vitamin K_1 and vitamin K_2 intakes in European population groups.

Objectives: The aim of this thesis was to estimate the intake, adequacy and dietary sources of vitamin K_1 and vitamin K_2 in nationally representative samples of the Irish population aged 1-90 years. A further aim was to investigate any changes in vitamin K_1 or vitamin K_2 intakes and sources in school-aged children between 2003-04 and 2017-18 using data from two nationally representative surveys of Irish children (5-12y), which used similar methodologies for dietary assessment. To facilitate estimation of these intakes, a key aim of this thesis was to update the Irish Food Composition Database (IFCD) (2012) with composition data for vitamin K_1 and vitamin K_2.

Methods: The IFCD (2012) consists of dietary data collected via weighed/semi-weighed food diaries during four national dietary surveys carried out by the Irish Universities Nutrition Alliance (www.iuna.net) over the last 20 years. These surveys included the National Pre-school Nutrition Survey (1-4y) (2010-11), the National Children's Food Survey (5-12y) (2003-04), the National Teens' Food Survey (13-17y) (2005-06) and the National Adult Nutrition Survey (18-90y) (2008-10). Each food and beverage consumed across these surveys were assigned a unique food code depending on its food descriptor and nutritional profile (*n* 3443). All food codes in the IFCD (2012) required a vitamin K_1, menaquinone-4 (MK-4) and menaquinone-5-10 (MK-5-10) composition value. As there are no analytical composition data available for vitamin K_1 or vitamin K_2 content of foods in Ireland, composition data were obtained from other analytical sources as this is considered to be an appropriate method for estimating nutrient content when direct analysis is not feasible. For vitamin K_1 and vitamin K_2, composition data were assigned to each food code using published analytical values from the UK Composition of Foods Integrated Dataset, the United

States Department of Agriculture National Nutrient Database or published papers, recipe calculation based on individual ingredients, and nutritional information on product labels. Foods that were either not fermented or not of animal origin were assigned a composition value of 0µg for all menaquinones. For a small number of food codes, vitamin K_1 values were assigned based on the fat content of a similar product or assigned a composition value of zero where no composition data were available. Using the updated composition data, the distribution of vitamin K_1 and vitamin K_2 intakes and adequacy (for vitamin K_1) in the Irish population were carried out using SPSS© for Windows™ Version 22.0. Differences in intakes of vitamin K_1 and vitamin K_2 between gender or age groups were assessed using independent sample T-tests. The percent contribution of each food group to the mean daily intake of vitamin $K_{1,}$ MK-4 and MK-5-10 was calculated by the mean proportion method.

Results: For vitamin K_1, 53% of food codes were assigned composition values from published analytical data, 31% were recipes calculated at ingredient level and 16% were assigned a value based on nutritional information on product labels or other methods. Herbs (213-3220µg/100g) and 'vegetable & vegetable dishes' (0-840µg/100g) were the most concentrated foods with vitamin K_1 in the database. For vitamin K_2, 48% of food codes were assigned a value of 0µg, 16% were assigned composition data from published analytical data, 25% were recipes calculated at ingredient level and 11% were assigned a composition value based on nutritional information on product labels or other methods. Foods highest in MK-4 were 'meat & meat products' (0-28µg/100g), 'eggs & egg dishes' (2.2-15µg/100g) and 'butter, spreading fats & oils' (0-15µg/100g). Foods highest in MK-5-10 were 'meat & meat products' (0-341µg/100g), 'cheese' (24-72µg/100g) and 'eggs & egg dishes' (0-28µg/100g).

Vitamin K_1 intakes and sources were estimated in Irish children aged 1-17 years. The key finding of this study was that the mean intakes of vitamin K_1 for Irish pre-school children (2.2µg/kg/d) and school-aged children (1.3µg/kg/d) were above the EFSA Adequate Intake (AI) of 1µg/kg/d (required to maintain normal blood coagulation). However, the mean vitamin K_1 intake for Irish teenagers (0.9µg/kg/d) was below the same AI. 'Vegetable & vegetable dishes' was the key source of vitamin K_1 (26%-32%), the majority of which was attributable to 'green vegetables' (15%-16%). The contribution from fruit to vitamin K_1 intake was higher in preschool children (14%), compared to school aged children and teenagers (4-7%). ‘Potatoes & potato products’ contributed 15-17% of vitamin K_1 intakes in the older age groups (5-12y and 13-17y).

Vitamin K_2 intakes and sources were estimated in the Irish population aged 1-90 years. Mean intakes of MK-4-10 ranged from 40-55µg/d (range across age group) in Irish children aged 1-17 years and from 42-58µg/d in adults 18-90 years. With regard to the individual menaquinones, mean intakes of MK-4 ranged from 8-13µg/d, with ‘meat & meat products’ (50-67%) and ‘milk’ (8-25%) the key sources of MK-4 across the population groups. Mean intakes of MK-5-10 ranged from 32-45µg/d, with ‘meat & meat products’ (44-61%) and ‘cheese’ (21-37%) the key sources of MK-5-10. Of the ‘meat & meat products’, sausages accounted for between 27-51% of MK-5-10 intakes.

There was no difference in the intake of vitamin K_1 or vitamin K_2 between 2003-04 and 2017-18. The key source of vitamin K_1 in both surveys was ‘vegetable & vegetable dishes’. ‘Meat & meat products’ was the key source of MK-4 and MK-5-10 in both studies.

Conclusion: Vitamin K_1 intakes in Irish children aged 1-4 and 5-12 years were 2.2 and 1.3µg/kg/d, respectively, which are above the AI of 1µg/kg/d set by EFSA to maintain normal blood coagulation however, intakes in teenagers aged 13-17 years (0.9µg/kg/d) were below the AI. ‘Vegetable & vegetable dishes’ was the key source of vitamin K_1 in Irish children of all age-groups (26-32%). For vitamin K_2, mean intakes of MK-4 and MK-5-10 ranged from 8-13µg/d and 32-45µg/d, respectively in the Irish population aged 1-90 years. ‘Meat & meat products’ was the key source of MK-4 (50-67%) and MK-5-10 (44-61%) in both children and adults in Ireland. For school-aged children, there was no difference in the intake or sources of vitamin K_1 or vitamin K_2 between 2017-18 and 2003-04. The data presented in this study will add to the small pool of data available on vitamin K_1 and vitamin K_2 intakes and sources in nationally representative samples of population groups. The Irish food composition database for vitamin K_1 and vitamin K_2 will support future researchers in the assessment of vitamin K intakes at individual or population level.

Chapter 1

Literature Review

Introduction

Vitamin K is the name given to a family of fat soluble compounds with a common chemical structure of 2-methyl 1,4-naphtoquinone but differ in the length and degree of saturation of their side chain (Shearer, 1995). Vitamin K consists of vitamin K_1 (phylloquinone) and vitamin K_2 (menaquinones). Vitamin K_1 contains a phytyl side chain of 4 prenyl units and is the primary form of vitamin K in the diet, present in all photosynthetic plants (Gross *et al.*, 2006, Shearer and Newman, 2008). Menaquinones contain an unsaturated side chain of varying length from 4 to 13 repeating isoprenoid units, denoted as MK-*n* where *n* signifies the number of isoprenoid units. Menaquinones are exclusively synthesized by bacteria (with the exception of menaquinone-4 (MK-4)) including bacteria capable of food fermentation and bacteria present in the human intestine, however, the contribution from gut derived menaquinones to vitamin K requirements is not yet fully understood (Conly *et al.*, 1994, Suttie, 1995, Karl *et al.*, 2017). MK-4 differs from the other menaquinones as is not produced by bacteria. It is formed in mammals from the tissue specific conversion from vitamin K_1 or menadione (which is a synthetic form of vitamin K that may be added to animal feed) (Dialameh *et al.*, 1971, Davidson *et al.*, 1998, EFSA Panel on Additives and Products or Substances used in Animal Feed, 2014). Consequently, menaquinones are found in foods of animal origin and fermented food products (Koivu-Tikkanen *et al.*, 2000, Schurgers and Vermeer, 2000, Manoury *et al.*, 2013, Vermeer *et al.*, 2018, Tarvainen *et al.*, 2019).

The bioavailability of vitamin K (and its individual components) from food is influenced by a number of factors including the form of the vitamin, the food matrix in which the vitamin is embedded, the presence of dietary fat and inter-individual differences (Gijsbers *et al.*, 1996, Booth *et al.*, 1997, Garber *et al.*, 1999, Schurgers and Vermeer, 2000, Schurgers *et al.*, 2007, Sato *et al.*, 2012).

The long standing metabolic function of vitamin K in the body is as a co factor for the enzyme gamma glutamyl carboxylase that catalyses the post translational carboxylation of glutamic acid residues into carboxyglutamic acid residues; this results in the activation of the Vitamin K Dependent (VKD) proteins which include proteins involved in blood coagulation (Suttie, 1992, Stafford, 2005). There is on-going evidence emerging for a role of vitamin K in extra hepatic functions, which include bone health, cardiovascular health, cognitive and anti-inflammatory functions (Booth, 2009, Vermeer, 2012, Halder *et al.*, 2019, Simes *et al.*, 2020). However, when the dietary supply of vitamin K is not sufficient to support all bodily functions, the carboxylation of VKD proteins involved in blood coagulation take priority over extra hepatic VKD proteins (McCann and Ames, 2009). This results in unfavourable levels of undercarboxylated extra hepatic Gla proteins such as osteocalcin (which plays a key role in bone metabolism) which have been reported in both adults and children globally (Binkley *et al.*, 2000, O'Connor *et al.*, 2007, Van Summeren *et al.*, 2007, Hayes *et al.*, 2016, Popko *et al.*, 2018). Improvements in the carboxylation of the VKD proteins have been reported from increased intakes of vitamin K in supplementation studies, suggesting that current dietary recommendations and intakes may not be sufficient for the carboxylation of all VKD proteins (Binkley *et al.*, 2000, Binkley *et al.*, 2002, Van Summeren *et al.*, 2009, Dalmeijer *et al.*, 2012, Theuwissen *et al.*, 2012, Knapen *et al.*, 2013, Knapen *et al.*, 2015).

This review aims to summarise the current dietary guidelines for vitamin K, sources of vitamin K composition data and dietary intakes and sources of vitamin K in nationally representative samples of population groups in Europe and the US. For inclusion in this review, data on vitamin K intakes had to be published in scientific reports or journal articles and the dietary data collected via food records or 24hr recalls or Food Frequency Questionnaires (FFQ). Food composition databases that contained values for vitamin K were identified by first examining the databases held by the European Food Information Resource (EuroFIR) followed by on-line searches for further data.

Dietary recommendations for vitamin K

Dietary recommendations for vitamin K are outlined in **Tables 1 and 2** and are summarised below.

The current recommendations for vitamin K across Europe and the US are generally for vitamin K_1 only and are based on its function in maintaining blood coagulation. The European Food Safety Authority (EFSA) (2017) has set an Adequate Intake (AI) of 1.0µg/kg/d for all age and sex population groups for vitamin K_1 only (EFSA Panel on Dietetic Products *et al.*, 2017). The AI of a nutrient is the average observed nutrient intake by a population group of apparently healthy people that is assumed to be adequate and is set when insufficient data are available to set an Estimated Average Requirement (EAR).

The Nordic Council of Ministers (NCM) (2014) recommend an intake of 1µg/kg/d of vitamin K_1 for adults and children (Nordic Council of Ministers, 2014).

In 2004, the World Health Organisation (WHO) set a Recommended Nutrient Intake (RNI) of 1µg/kg/d of vitamin K_1 for all age groups (WHO/FAO, 2004). The RNI is the amount of a nutrient that ensures the needs of nearly all the population (97.5%) are being met.

The US Institute of Medicine (IOM) (2001) has set an AI for vitamin K for adults and children based on the highest median intake of vitamin K (assumed to be vitamin K_1) observed in the US National Health and Nutrition Examination Survey III (Institute of Medicine, 2001). The AI for children aged 1-3 and 4-8 years was set at 30 and 55µg/d, respectively. For older children aged 9-13 and 14-18 years, the AI was 60 and 75µg/d, respectively. The AI for men and women of all ages was set at 120 and 90µg/d, respectively.

The UK Department of Health (DoH) (1991) reported that intakes of 1µg/kg/d of vitamin K_1 seemed safe and adequate for adults. The DoH did not provide a guideline for children (Department of Health, 1991).

For vitamin $K_{2,}$ the EFSA stated that there is currently uncertainties surrounding the function, content and metabolism of the menaquinones in the body and consequently recommendations for vitamin K_2 cannot be set (EFSA Panel on Dietetic Products *et al.*, 2017).

Table 1. Dietary reference values for vitamin K for adults in Europe and the US

	European Food Safety Authority[1] (2017)*	**Nordic Council of Ministers[2] (2014)**	**World Health Organisation[3] (2004)***	**Institute of Medicine[4] (2001)**	**Department of Health[5] (1991)**
Age	≥ 18	≥ 18	>18	>18	≥18
Men (µg/d)	70	1**	65	120	1**
Women (µg/d)	70	1**	55	90	1**

*Based on intake of 1µg per kg body weight per day

**µg per kg body weight per day

[1] EFSA Panel on Dietetic Products *et al.* (2017)

[2] Nordic Council of Ministers (2014)

[3] WHO/FAO (2004)

[4] Institute of Medicine (2001)

[5] Department of Health (1991)

Table 2. Dietary reference values for vitamin K for children in Europe and the US

	Age	µg/d
European Food Safety Authority[1] (2017)*	1-3 years	12
	4-6 years	20
	7-10 years	30
	11-14 years	45
	15-17 years	65
World Health Organisation[2] (2004)*	1-3 years	15
	4-6 years	20
	7-9 years	25
	10-18 years	35-55
US Institute of Medicine[3] (2001)	1-3 years	30
	4-8 years	55
	9-13 years	60
	14-18 years	75

*Based on intake of 1µg per kg body weight per day

[1] EFSA Panel on Dietetic Products *et al.* (2017)

[2] WHO/FAO (2004)

[3] US Institute of Medicine (2001)

Food Composition data for vitamin K_1 and vitamin K_2

Country specific food composition databases that report the vitamin K content of foods are outlined in **Table 3** and summarised in this section.

Food composition databases are necessary for the estimation of nutrient intakes in population groups and are the foundation behind national dietary surveys and epidemiological research (Williams, 2005). Composition databases reporting the vitamin K content of foods are limited throughout Europe and further afield (Shearer and Bolton-Smith, 2000, Elmadfa and Meyer, 2010) and the EFSA have recently highlighted the need for analytical data reporting the vitamin K_1 and vitamin K_2 content of foods (EFSA Panel on Dietetic Products *et al.*, 2017).

In order to compile a list of composition databases reporting the vitamin K (vitamin K_1, vitamin K_2 or total vitamin K) content of foods, composition databases listed in the European Food Information Resource (EuroFIR) were reviewed for vitamin K composition data. EuroFIR is an international, independent broker that validates and encourages the use of food composition data in research and industrial environments. Of the 27 composition databases reviewed on EuroFIR, 10 composition databases included the vitamin K content of foods, the majority of which were not comprehensive and were missing data. The UK Composition of Foods Integrated Dataset (COFID) reported the vitamin K_1 composition of foods analysed directly and using published analytical data from a 'provisional' composition database reported by Bolton-Smith *et al.* (2000) (Public Health England Composition of Foods Integrated Dataset, 2015). Analytical values for the MK-4 composition of eggs were also included in the UK COFID (Public Health England Composition of Foods Integrated Dataset, 2015). The United States Department of Agriculture (USDA) National Nutrient Database analysed the vitamin K_1 composition of a wide variety of foods and the MK-4 composition of predominantly meats and foods of animal origin (USDA National Nutrient Database for Standard References Release 28, 2015). Other food composition databases as discussed below include vitamin K values derived using a combination of methods including obtaining analysed data from other countries or from the literature, estimating values via recipe calculation or applying values based on that of similar foods. Composition databases report vitamin K composition in this manner in Denmark and Germany (for vitamin K_1), in France and Turkey (for vitamin

K_1 and K_2), in Finland, Sweden and the Netherlands (for total vitamin K) and in Italy (for vitamin K_1, MK-4 and dihydrophylloquinone (formed from the hydrogenation of vitamin K_1 rich oils) (Technical University of Denmark, 2007, Anses/CIQUAL, 2013, TürKomp Turkish Food Composition Database, 2014, Food Composition Database Italy (BDA), 2015, Dutch Nutrients Database (NEVO), 2016, German Food Code and Nutrient Database, 2017, Swedish National Food Database, 2017, Finnish National Food Composition Database, 2019).

In addition, some researchers have compiled vitamin K composition databases that include vitamin K composition data for a number of foods based on published analytical values, recipe calculation and similar vitamin K content of another product. Examples of these include databases of vitamin K_1 for UK foods by Bolton-Smith *et al.* (2000) and for US foods by Booth *et al.* (1993). Both studies reported the vitamin K_1 content of vegetables, fruits, grains and cereals, beverages, dairy and meats. Vegetables, especially green vegetables, were consistently reported as highly concentrated with vitamin $K_{1.}$ However, it is important to note that there may be variations in the vitamin K_1 content of green vegetables depending on the level of maturation of the vegetable and the layer or part of the vegetable analysed (Ferland and Sadowski, 1992b). Other smaller studies reporting the vitamin K_1 content of foods have highlighted that herbs and some oils are high in vitamin K_1, which consequently increase the vitamin K_1 content of mixed dishes and food products (such as salad dressings and condiments) in which they are added as ingredients (Peterson *et al.*, 2002, Dumont *et al.*, 2003, Presse *et al.*, 2015, Finnan *et al.*, 2017). As vitamin K_1 is highly sensitive to light, there may be a decrease in the vitamin K_1 content of commonly consumed oils of over 90% if exposed to daylight/fluorescent light (Ferland and Sadowski, 1992a). The vitamin K_1 content of nuts and fruits were reported in a small study in the US with the majority of these foods containing low concentrations of vitamin K_1 with the exception of some berries and green fruits (Dismore *et al.*, 2003). Vitamin K_1 has also been reported in low concentrations in meat, poultry and dairy, and in grains such as rice, pasta and cereals in smaller studies in Europe and the US (Schurgers and Vermeer, 2000, Elder *et al.*, 2006, Ferreira, 2006, Fu *et al.*, 2017).

For total and/or individual menaquinones, there are limited composition data included in composition databases. MK-4 is found in foods of animal origin due to the tissue specific conversion of menadione present in animal feed or from phylloquinone (Thijssen *et al.*, 2006, Okano *et al.*, 2008). MK-4 composition data has been reported for a small number of foods in Europe and the US (Koivu-Tikkanen *et al.*, 2000, Schurgers and Vermeer, 2000, Elder *et al.*, 2006, Ferreira, 2006, Manoury *et al.*, 2013, Fu *et al.*, 2016, Finnan *et al.*, 2017, Fu *et al.*, 2017, Vermeer *et al.*, 2018).

The longer chained menaquinones (MK-5-13) are exclusively synthesized by bacteria including bacteria capable of food fermentation and thus the concentration and forms of the menaquinones present in a food are highly dependent on the starter culture used and the fermentation conditions (Walther *et al.*, 2013). Analytical data for foods in Europe and the US have highlighted high concentrations of the longer chained menaquinones in dairy products, especially cheese, and fermented foods and a recent study in the US was the first to report high concentrations of menaquinone forms, specifically MK-10, in processed pork products (Koivu-Tikkanen *et al.*, 2000, Schurgers and Vermeer, 2000, Manoury *et al.*, 2013, Fu *et al.*, 2016, Fu *et al.*, 2017, Tarvainen *et al.*, 2019).

Dietary intakes

Vitamin K_1 intakes and sources in children

The intakes and sources of vitamin K_1 in nationally representative samples of children are outlined in **Table 4** and are summarised in this section. Vitamin K_1 intake data is available in national surveys for children in Ireland, the UK, Austria, Greece (assumed to be vitamin K_1) and the US, with intakes ranging from 24-79µg/d in children aged 4-19 years. There were differences in dietary assessment methodologies used between countries and estimated intakes were reported as either mean intake (Irelands, Austria & the US), geometric mean (UK), or usual intakes (Greece).

Preliminary vitamin K_1 intakes and sources (using limited composition data) in Irish children aged 5-12 years (*n* 594) were estimated using dietary data collected via a 7-day weighed food record during the National Children's Food Survey (NCFS) (2003-04) (Hannon *et al.*, 2007). Mean vitamin K_1 intake in girls aged 5-8 and 9-12 years was 36.7 and 39.7µg/d, respectively. Mean vitamin K_1 intake in boys aged 5-8 and 9-12 years was 34.2 and 41.0µg/d, respectively. 'Vegetables & vegetables dishes' was the key source of vitamin K_1 (30%), followed by 'potatoes & potato products' (14%) and 'meat & meat products' (10%).

The intakes and sources of vitamin K_1 in 4 year old British children between 1950 and the 1990s were compared using data from the longitudinal Medical Research Council National Survey of Health and Development (1950) (NSHD) and the National Diet and Nutrition Surveys (1992/3 and 1997) (NDNS) (Prynne *et al.*, 2005). The NSHD used a 24h recall to collect dietary data whilst the NDNS used a 4-day and a 7-day weighed food diary in 1992/3 and 1997, respectively. Geometric mean vitamin K_1 intakes of 4-year-old children in the 1950s (*n* 4411) and 1990s (*n* 291) were 39µg/d (or 2.3µg/kg/d) and 24µg/d (or 1.4µg/kg/d), respectively. The contribution from vegetable and vegetable products was significantly higher in 1950 compared to the 1990s (60% vs 48%), primarily due to the decrease in the consumption of green leafy vegetables from 1950 to the 1990s. Potatoes, meat, fish and their products and biscuits, cakes and pastries made a higher contribution to the mean intake of vitamin K_1 in the 1990s compared to the 1950s.

The Austrian Dietary Survey (2012) collected dietary data from 163 girls and 169 boys aged 7-14 years using a 3-day food record (Elmadfa *et al.*, 2012). Mean vitamin K_1 intakes were reported for girls and boys aged 7-9 years (girls; 75µg/d, boys; 67µg/d), 10-12 years (girls: 59µg/d, boys: 71µg/d) and 13-14 years (girls: 61µg/d, boys: 69µg/d). Sources of vitamin K_1 were not reported.

The GENESIS study (2003-2004) assessed the nutrient intake of a representative sample of pre-school children in Greece aged 1-5 years (*n* 2374) using a 3-day food record (2 consecutive weekdays and 1 weekend day) (Manios *et al.*, 2008). The usual intake of vitamin K (assumed to be vitamin K_1) was 32.2µg/d. Sources of vitamin K were not reported.

Mean vitamin K_1 intakes were reported by the National Health and Nutrition Examination Survey (NHANES) (2015-2016) in the US with the collection of dietary intake data using 2x24hr recalls (US Department of Agriculture, 2018). For girls aged 2-5, 6-11 and 12-19 years, mean vitamin K_1 intakes were 48.2, 62.8 and 73.9 µg/d, respectively. Mean vitamin K_1 intakes for boys aged 2-5, 6-11 and 12-19 years were 55.4, 62.9 and 78.6µg/d, respectively. Sources of vitamin K_1 were not reported.

Vitamin K_1 intakes and sources in adults

The intake and sources of vitamin K_1 in nationally representative samples of adults are outlined in **Table 5** and are summarised in this section. Vitamin K_1 intake data are available in national surveys for adults in Ireland, the UK, Austria, Germany, Spain, the US and Korea, with intakes ranging from 45-243µg/d in adults aged 15->90 years. Similar to that previously outlined for children and teenagers, there were differences in dietary assessment methodologies used between countries and intakes were reported as either mean (Ireland, Austria, the US & Spain), geometric mean (UK) or median (Germany).

Dietary data collected during the National Adult Nutrition Survey (NANS) (2008-10) of adults 18-90 years and the North/South Ireland Food Consumption Survey (NSIFCS) (1997-99) of adults aged 18-64 years have reported the vitamin K_1 intakes and sources in nationally representative samples of adults in Ireland (Duggan *et al.*, 2004, Hayes *et al.*, 2016). Habitual food and beverage intake data was collected using a 4-day semi weighed food record in the NANS (*n* 1500) and a 7-day weighed food record in the NSIFCS (*n* 1379). The mean intake of vitamin K_1 in the NANS was reported by gender for adults aged 18-35 years (women: 71.3µg/d, men: 79.8µg/d), 36-50 years (women: 86.2µg/d, men: 86.7µg/d), 51-64 years (women: 97.8µg/d, men: 97.9µg/d) and >65 years (women: 91.5µg/d, men: 83.4µg/d) (Hayes *et al.*, 2016). The mean intake of vitamin K_1 in the NSIFCS was reported by gender for adults aged 18-35 years (women: 75.2µg/d, men: 77.6µg/d), 36-50 years (women: 78.3µg/d, men: 89.3µg/d) and 51-64 years (women: 81.7µg/d, men: 86.8µg/d) (Duggan *et al.*, 2004). Overall, there was no difference in mean intake of vitamin K_1 in adults 18-50 years between 2008-10 and 1997-99 however, intakes increased significantly ($P = 0.009$) in the 51-64 year age group over the 10-year period. For both the NANS and the NSIFCS, vegetable and vegetable dishes were the key source of vitamin K_1 (44-49%), of which green vegetables contributed 25-33%. Meat and meat products (6-10%), potato and potato products (4-10%) and dairy and fat spreads (7-12%) were important contributors to intakes of vitamin K_1 in both the NANS and the NSIFCS.

The geometric mean intake of vitamin K_1 in British adults aged 16-64 years significantly decreased in 2000-01 compared to the national nutrition survey in 1986-87 (Thane *et al.*, 2006a). A 7-day weighed food diary was used to collect dietary data in the Dietary and Nutrition Survey of British adults aged 16-64 years in 1986-1987 (*n* 1916) and the National Diet and Nutrition Survey (NDNS) of adults aged 19-64 years in 2000-01 (*n* 1423). The geometric mean vitamin K_1 intake in adults from the UK aged 16-64 years in 1986-87 was 72µg/d (1µg/kg/d) and 67µg/d (0.9µg/kg/d) in

2000-01. In 1986-87, geometric mean vitamin K_1 intakes were reported for adults aged 16-34 years (women: 53µg/d, men 70µg/d), 35-44 years (women: 66µg/d, men: 82µg/d), 45-54 years (women: 75µg/d, men: 89µg/d) and 55-64 years (women: 76µg/d, men 90µg/d). In 2000-01, geometric mean vitamin K_1 intakes were reported for adults aged 19-34 years (women: 51µg/d, men: 59µg/d), 35-44 years (women: 62µg/d, men: 68µg/d), 45-54 years (women: 73µg/d, men: 82µg/d) and 55-64 years (women: 79µg/d, men: 83µg/d). Vegetable and vegetable dishes were the top contributor to intakes in both surveys (60-63%). Of this, leafy green vegetables accounted for 19-23% of vitamin K_1 intakes. Cereal and cereal products contributed 11% of vitamin K_1 intakes across both surveys followed by meat and meat products (6-8%) and fat spreads (4%).

The intakes and sources of vitamin K_1 were also reported in a national sample of British elderly (>65 years) (*n* 1091) according to socio- demographic and lifestyle factors (Thane *et al.*, 2002b). Dietary data was collected via a 4-day weighed diary in the NDNS 1994-95. Geometric mean vitamin K_1 intake was 61µg/d (0.99µg/kg/d) and 70µg/d (0.94µg/kg/d) for women and men, respectively. Stratified by age, intakes were 66µg/d, 57µg/d and 45µg/d in women aged 65-74, 75-84 and >85 years, respectively. Stratified by age, intakes were 72µg/d, 68µg/d, and 54µg/d in men aged 65-74, 75-84 and >85 years, respectively. Vegetable and vegetable products were the key source of vitamin K_1 (60%), of which, green vegetables accounted for 28%. Other important sources of vitamin K_1 were cereals (12%), meat (7%) and fat spreads (4%).

The German National Nutrition Survey II (2007-10) reported median vitamin K_1 intake of 76µg/d in adults aged 15-80 (*n* 6160) years using two 24hr recalls to collect dietary data (Deutsche Gesellschaft fur Ernahrung, 2012).

The mean intake of vitamin K_1 in a representative sample of Spanish adults (*n* 1068) aged 17-60 years using a 3-day diary to collect dietary data was 170.2µg/d (Ortega Anta *et al.*, 2014). Split by gender, mean vitamin K_1 intake was 166.4 and 174.2µg/d for women and men, respectively. The key contributors to vitamin K_1 intake were vegetables (45%), fats and oils (13%), pulses (12%), meat (10%), cereals (5%) and fruits (5%).

Mean vitamin K_1 intakes reported by the NHANES in the US collected dietary intake data using 2x24hr recalls for adults greater than 20 years with vitamin K_1 intakes of

123.5 and 118.2µg/d for women and men, respectively (US Department of Agriculture, 2018). Sources of vitamin K_1 were not reported.

The Austrian Dietary Survey (2012) collected dietary data via two 24hr recall for adults aged 18-80 years (*n* 556) (Elmadfa *et al.*, 2012). Mean vitamin K_1 intakes were reported for adults aged 18-24 years (women: 109g/d, men: 114µg/d), 25-50 years (women: 102g/d men: 89µg/d,), 51-64 years (women: 93 µg/d, men: 93µg/d) and 65-80 years (women; 117g/d, men; 108µg/d). Sources of vitamin K_1 were not reported.

The Korea National Health and Nutrition Examination Survey (2010-2011) collected dietary data using a 24hr recall in 2,785 men and 4,307 women greater than 19 years (Kim *et al.*, 2015). Vitamin K_1 intake was 243µg/day and 200µg/day for adult men and women, respectively. Higher intakes of vitamin K_1 in the Korean population are due to the consumption of foods that are high in vitamin K_1 such as natto and misso.

Vitamin K_2 intakes and sources

To the best of this author's knowledge, there are no nationally representative dietary surveys that report intakes of vitamin K_2 in adults or children in Europe or the US. Studies that report the intakes of vitamin K_2 were predominantly investigating the association of menaquinones with specific health outcomes and are summarised in this section.

The relationship between dietary menaquinones and disease incidence was investigated using data from the European Prospective Investigation into Cancer and Nutrition (EPIC), which collected dietary data via a semi- quantitative FFQ (Nimptsch *et al.*, 2008, Beulens *et al.*, 2009, Gast *et al.*, 2009, Beulens *et al.*, 2010, Nimptsch *et al.*, 2010, Vissers *et al.*, 2013, Zwakenberg *et al.*, 2017). These studies investigated menaquinone intake (ranging from MK-4 to MK-14 with variations between studies) and their association with specific disease outcomes in different cohorts of the EPIC study. In general, intakes of the menaquinones in these studies were 29-35µg/d. Sources of menaquinones were reported in two of these studies, (which used dietary data from the EPIC study) with dairy products (60%), especially cheese (43-53%), and meat and meat products (17%) found to be the key contributors to intakes of the menaquinones (Nimptsch *et al.*, 2008, Beulens *et al.*, 2010).

The Hordaland Healthy Study (1997-2000) collected dietary intake data in Norway from men and women born in 1925-1927 and 1950-1951 using a 169 item FFQ and this dietary data was used to analyse the intakes of vitamin K_2 and the risk of bone mineral density and hip fracture (Apalset *et al.*, 2010, Apalset *et al.*, 2011). Intakes of vitamin K_2 and its association with bone mineral density ranged from 11.6-15.6 and 13.2-18.0µg/d in Norwegian women and men aged 47-75 years, respectively (Apalset *et al.*, 2010). In an investigation into the association between vitamin K_2 intakes and the risk of hip fracture in adults aged 71-75 years, vitamin K_2 intakes were 10.8 and 11.9µg/d for women and men with no hip fracture, respectively (Apalset *et al.*, 2011).

Geleijnse *et al.* (2004) reported the dietary intake of menaquinones and their association with a reduced risk of coronary heart disease for participants of The Rotterdam Study (1990-1993). Dutch men and women ≥55 years with dietary data and no history of myocardial infarction at baseline were included in the analysis for menaquinone intake (*n* 4807). Dietary data was collected at the time of the Rotterdam Study via a validated semi-quantitative FFQ. For women, intakes were 6.3 and 20.7µg/d for MK-4 and MK-5-10, respectively. Intakes of MK-4 and MK-5-10 were 7.7 and 23.1µg/d for men, respectively.

Total vitamin K intakes and sources in children and adults

The intakes and sources of total vitamin K in nationally representative samples of adults and children are outlined in **Table 6** and are summarised in this section. Total vitamin K intake data are available in national surveys for children in Belgium, the Netherlands, Finland and Germany with intakes ranging from 54-409µg/d in children aged 3-18 years (Mensink *et al.*, 2007, Hoppu *et al.*, 2010, Buurma-Rethans and Van Rossum, 2015, Moyersoen *et al.*, 2017). In adults, total vitamin K intake data are available in Belgium, the Netherlands and Finland with intakes ranging from 87-185µg/d in adults aged 18-96 years (Helldán *et al.*, 2013, Buurma-Rethans and Van Rossum, 2015, Moyersoen *et al.*, 2017). However, there are uncertainties and inconsistencies on the forms of vitamin K included within the ‘total vitamin K’ estimation between countries. The EFSA also reported an overview of total vitamin K intakes using dietary data from 13 dietary surveys with intakes ranging from 36-143 and 72-196µg/d in children aged 1-<18 and adults greater than 18 years, respectively (EFSA Panel on Dietetic Products *et al.*, 2017). Different methods of dietary assessment were used between countries and intakes were reported as either mean (the Netherlands, Finland, Germany), or usual intakes (Belgian).

In 2017, the EFSA published its scientific opinion on dietary reference values for vitamin K (EFSA Panel on Dietetic Products *et al.*, 2017). During this study, the panel aimed to report the observed total vitamin K intakes using food consumption and composition data provided to EFSA from 13 dietary surveys across 9 countries. Although total vitamin K refers to the sum of vitamin K_1 and vitamin K_2, this may vary by country depending on the available food composition data and therefore, it should be noted that EFSA have outlined large uncertainties in the food composition data (whether vitamin K_1 only or the sum of vitamin K_1 and vitamin K_2) used to calculate total vitamin K intake. Mean total vitamin K intakes were 36-53µg/d and 42-93 µg/d in children 1-<3 and 3-<10 years, respectively. Mean total vitamin K intakes in children 10-<18 years were 68-143µg/d and 72-196µg/d in adults greater than 18 years. Vegetable and vegetable products were the key source of total vitamin K intakes. Composite dishes were also important contributors to intakes of total vitamin K due to the ingredients included in the composite dish (vegetables, fats and oils, nuts and legumes food group).

Data from the Belgian Food Consumption Survey (2014) was used to estimate usual intakes and sources of total vitamin K for 3200 participants aged 3-64 years (Moyersoen *et al.*, 2017). Dietary data was collected using two non-consecutive 24hr dietary recalls and a self-administered FFQ for participants aged 10-64 years. For children aged 3-9 years, two non-consecutive one-day food diaries and a self-administered FFQ was used to collect dietary data. Total vitamin K intakes for girls aged 3-6, 7-10 and 11-14 years were 54, 58 and 65µg/d, respectively. Total vitamin K intakes for boys aged 3-6, 7-10 and 11-14 years were 64, 63 and 69µg/d, respectively. Total vitamin K intakes for adolescents aged 15-17 years were 71 and 76µg/d for girls and boys, respectively. For adults aged 18-39 years, intakes were 108 and 111µg/d for women and men, respectively. Total vitamin intakes at age 40-64 years were 176 and 185µg/d for women and men, respectively. Vegetables (54%) were the top contributor to intakes in the Belgian population followed by dairy products (16%), fruits and nuts (11%), fats and oils (9%), sauces, spices and herbs (3.8%) and supplements (0.9%).

The Dutch National Survey (2007-10) collected dietary data via 2 non-consecutive 24hr dietary recalls and reported mean intakes of total vitamin K (based on vitamin K in vegetables, fruit, legumes and dairy products only) in 3189 children and adults aged 7-69 years in a memo (Buurma-Rethans and Van Rossum, 2015). Mean total vitamin

K intakes were 70 and 80µg/d in girls and boys aged 7-18 years, respectively. Mean total vitamin K intakes were 111 and 128µg/d in women and men aged 19-96 years, respectively.

FINDIET 2012 reported the mean daily intake of total vitamin K in Finnish adults aged 25-74 years using a 48hr recall (Helldán *et al.*, 2013). Mean total vitamin K intakes for women and men aged 25-64 years were 95 and 104µg/d, respectively. Mean total vitamin K intakes for women and men aged 65-74 years were 87 and 99µg/d, respectively. Vegetables contributed 33-40% to the mean intake of total vitamin K followed by fats (24-30%) and meat (8-12%).

A cross sectional study in Finnish seventh grade pupils in 2007 collected food and nutrient intake data using questionnaires to assess dietary habits and patterns in 726 pupils and a computer assisted 48h recall in a sub group of 306 pupils to estimate nutrient intake (Hoppu *et al.*, 2010). Students had a mean age of 13.8 years and a mean total vitamin K intake of 77 and 82µg/d for girls and boys, respectively.

The EsKiMo study in Germany assessed the dietary intake of a representative sample of children aged 6 to 17 years (*n* 2644) using a 3-day dietary record (Mensink *et al.*, 2007). Mean total vitamin K intakes in children aged 6, 7-9 and 10-11 years were 152-173, 183-199 and 193-206µg/d, respectively. Mean total vitamin K intakes in children aged 12, 13-14 and 15-17 years were 316-320, 328-344 and 340-409µg/d, respectively. It should be noted that these data appear to overestimate vitamin K intakes in German children possibly due to the composition data that were used (EFSA Panel on Dietetic Products *et al.*, 2017).

Mean total vitamin K intake was estimated in Japanese women aged 20-23 years (*n* 125) enrolled at Kagawa Nutrition University using dietary data collected over 3 days (Kamao *et al.*, 2007). Mean total vitamin K intake was 230.2µg/d. Key sources of total vitamin K in this age group were pulses (including fermented soybean products) (45%) and vegetables (38%).

Other relevant studies

The intake of vitamin K_1 and vitamin K_2 was reported in 5435 adults greater than 55 years that participated in the Rotterdam study (Geleijnse *et al.*, 1999). Dietary data was collected using a semi-quantitative FFQ. Vitamin K_1 intake in the total population was 249µg/d. Split by gender; intakes were 244 and 257µg/d for women and men, respectively. Vitamin K_2 intakes were reported for both MK-4 and the higher menaquinones (MK-5-10). Intakes of MK-4 and MK-5-10 in the total population were 6.8 and 21.6µg/d, respectively. For women (*n* 3210), intakes of MK-4 and MK-5-10 were 6.3 and 20.6µg/d, respectively. For men (*n* 2225), intakes were 7.5 and 22.9µg/d for MK-4 and MK-5-10, respectively.

The dietary intake of vitamin K_1 was reviewed in 11 different studies of adults greater than 18 years with results published between 1988 and 1997 (Booth and Suttie, 1998). Across all studies, mean intakes of vitamin K_1 were consistently higher in older adults >55 years (80-210µg/d) than mean intakes in younger adults <45 years (60-110µg/d), primarily due to a higher consumption of vegetables in older adults.

Biomarkers of vitamin K status

Vitamin K deficiency can be evaluated using coagulation tests such as prothrombin time (PT) or activated partial thromboplastin time (APTT). However, they are not sensitive measures of vitamin K status as they do not reflect all the roles of vitamin K in the body and are not appropriate to assess vitamin K status in population studies (Booth and Al Rajabi, 2008, Shea and Booth, 2016). Although there is an association between dietary intake of phylloquinone and phylloquinone plasma concentrations, this only reflects recent dietary intake and has large 'within subject' variation (Booth *et al.*, 1997, Sokoll *et al.*, 1997, Booth *et al.*, 1999, Thane *et al.*, 2002a, Thane *et al.*, 2006b). Similarly, depletion and repletion studies with VKD proteins have highlighted rapid changes in plasma concentrations in response to dietary changes and therefore cannot be used as a gold standard measure of vitamin K status (Ferland *et al.*, 1993, Sokoll *et al.*, 1997, Binkley *et al.*, 2000, Booth *et al.*, 2003)

Therefore it can be concluded that for vitamin K there is currently no biomarker or no optimal level of gamma carboxylation that can be used as a cut off to define vitamin K adequacy (EFSA NDA Panel, 2017).

Conclusion

This review aimed to examine the current dietary recommendations available for vitamin K, sources of vitamin K composition data and dietary intakes and sources of vitamin K in nationally representative samples of population groups in Europe and the US. A review of the available dietary reference values for vitamin K_1 has shown that the recommendation for both adults and children is typically 1µg/kg body weight per day even though different dietary reference values have been used to set this value. For vitamin K_2, there is currently insufficient knowledge available on the function, content and bioavailability of menaquinones in the body to set a dietary reference value for vitamin K_2. There are limited composition data available for vitamin K and its separate components. Of the 27 composition databases reviewed on EuroFIR, 10 composition databases included data on the vitamin K content of foods. The majority of these composition databases were not complete for all foods but included published analytical data from other countries, values based on similar foods and calculated values from recipes for a number of foods.

Total vitamin K intakes were reported in a number of European studies with intakes in children and adults typically ranging from 54-82µg/d and 87-185µg/d, respectively. Of the studies that reported sources of total vitamin K, 'vegetables & vegetable dishes' (33-54%) was the key source.

Vitamin K_1 intakes in nationally representative samples of children and adults across Europe and the US generally ranged from 24-79µg/d and 45-174µg/d, respectively, with 'vegetable & vegetable dishes' the key source of vitamin K_1 (29-63%). Data on vitamin K_2 intakes were not available in national dietary surveys however, vitamin K_2 intakes from other studies generally ranged from 12-35µg/d with dairy products (60%), especially cheese (43-53%), and meat and meat products (17%) the key sources of vitamin K_2.

Table 3. Overview of composition databases reporting vitamin K composition data by country

Country	**Form of vitamin K**
Denmark[1]	Vitamin K_1
Finland[2]	Total vitamin K
France[3]	Vitamin $K_{1,}$ vitamin K_2
Germany[4]	Vitamin K_1
Italy[5]	Vitamin K (vitamin K_1, MK-4 and dihydrophylloquinone)
Netherlands[6]	Total vitamin K
Sweden[7]	Total vitamin K
Turkey[8]	Vitamin $K_{1,}$ vitamin K_2
United Kingdom[9]	Vitamin $K_{1,}$ menaquinone-4
America[10]	Vitamin $K_{1,}$ menaquinone-4

[1] Technical University of Denmark (2007),

[2] Finnish National Food Composition Database (2019)

[3] Anses/CIQUAL (2013)

[4] German Food Code and Nutrient Database (2017)

[5] Food Composition Database Italy (BDA) (2015)

[6] Dutch Nutrients Database (NEVO) (2016)

[7] Swedish National Food Database (2017)

[8] TürKomp Turkish Food Composition Database (2014)

[9] Public Health England Composition of Foods Integrated Dataset (2015)

[10] USDA National Nutrient Database for Standard References Release 28 (2015)

Table 4. Overview of national dietary surveys reporting the intakes and sources of vitamin K_1 in children

Country	Study Name	Study years	Dietary assessment method	Age (years)	Intakes μg/d	Sources
Ireland[1]	National Children's Food Survey	2003-04	7-day diary	5-8	36.7 (girls), 34.2 (boys)	Vegetable& vegetable dishes (29%)
				9-12	39.7 (girls), 41.0 (boys)	Potatoes & potato products (14%) Meat & meat products (10%)
Austria[2]	Austrian Nutrition Report	2010-12	3-day diary	7-9	75 (girls), 67 (boys)	Not provided
				10-12	59 (girls), 71 (boys)	
				13-14	61 (girls), 69 (boys)	
Greece[3]	The genesis study	2003-04	3-day diary	1-5	32.2	Not provided
United States[4]	National Health and Nutrition Examination Survey	2015-16	2*24h recall	2-5 6-11 12-19	48.2 (girls), 55.4 (boys) 62.8 (girls), 62.9 (boys) 73.9 (girls), 78.6 (boys)	Not provided
United Kingdom[5]	Longitudinal Medical Research Council National Surveys of Health and Development	1950	24hr dietary recall	4	39	Vegetable & vegetable dishes (60%)
	National Diet and Nutrition Survey	1992/93-97	4-day/7-day weighed diary	4	24	Vegetable & vegetable dishes (48%)

[1] Hannon *et al.* (2007) [2] Elmadfa *et al.* (2012), [3] Manios *et al.* (2008), [4] US Department of Agriculture (2018), [5] Thane *et al.* (2006a)

Table 5. Overview of national dietary surveys reporting the intakes and sources of vitamin K_1 in adults

Country	Study Name	Dietary assessment method	Study years	Age (years)	Intakes µg/d (females)	Intakes µg/d (males)	Sources
Austria[1]	Austrian Nutrition Report	3-day diary	2010-12	18-24	109	114	Not provided
				25-50	102	89	
				51-64	93	93	
				65-80	117	108	
Ireland[2]	National Adult Nutrition Survey	4-day semi weighed diary	2008-10	18-90	84.4	86.0	Vegetable & vegetable dishes (44-49%)
				18-35	71.3	79.8	Meat & meat products (6-10%)
				36-50	86.2	86.7	Potatoes & potato products (4-8%)
				51-64	97.8	87.9	Dairy & fat spreads (10-12%)
				>65	91.5	83.4	
	North South Ireland Food Consumption Survey	7-day weighed diary	1997-99	18-64	75.2	84.2	
				18-35	75.2	77.6	Vegetable & vegetable dishes (48%)
				36-50	78.3	89.3	Potatoes & potato products (10%)
				51-64	81.7	86.8	Dairy & fat spreads (10%)
Germany[3]	German National Nutrition Survey II	2*24h recall	2005-07	15-80	76 (Total)		Not provided
Spain[4]		3x FFQ		17-60	166.4	174.2	Vegetables (45%)
							Fats and oils (13%)
United Kingdom[5]	Dietary and Nutritional Survey of British Adults	7-day weighed diary	1986-87	16-64	64	80	Vegetable & vegetable dishes (63%)
				16-34	53	70	Cereals & cereals products (11%)
				35-44	66	82	
				45-54	75	89	
				55-64	76	90	

	National Diet and Nutrition Survey	7-day weighed diary	2000-01	19-64	64	71	Vegetable & vegetable dishes (60%)
				19-34	51	59	Cereals & cereals products (11%)
				35-44	62	68	
				45-54	73	82	
				55-64	79	83	
United Kingdom[6]	National Diet and Nutrition Survey	4-day weighed diary	1994-95	>65	61	70	Vegetable & vegetable products (60%)
				65-74	66	72	Cereals (12%)
				75-84	57	68	Meat (7%)
				>85	45	54	Fat spreads (4%)
United States[7]	National Health and Nutrition Examination Survey	2 x 24hr dietary recalls	2015-16	>20	123.5	118.2	Not provided
Korea[8]	The Korea National Health and Nutrition Examination Survey	24hr recall	2010-2011	>19	200	243	Not provided

[1] Elmadfa *et al.* (2012), [2] Hayes *et al.* (2016), [3] Deutsche Gesellschaft fur Ernahrung (2012), [4] Ortega Anta *et al.* (2014), [5] Thane *et al.* (2006a), [6] Thane *et al.* (2002a) [7] US Department of Agriculture (2018), [8] (Kim *et al.*, 2015)

Table 6. Overview of national dietary surveys reporting the intakes and sources of total vitamin K in adults and children

Country	Study Name	Study years	Dietary assessment method	Age (years)	Intakes µg/d (females)	Intakes µg/d (males)	Sources
Belgium[1]	Belgium National Food Consumption Survey[1]	2014-2015	2*24h recall	3-6	54	64	Vegetables (54%)
				7-10	58	63	Dairy products (16%)
				11-14	65	69	Fruits and nuts (11%)
				15-17	71	76	Fats and oils (9%)
				18-39	176	111	Sauces, spices & herbs (3.8%)
				40-64	176	185	Supplements (0.9%)
The Netherlands[2]	Dutch National Survey	2007-10	2*24h recall	7-18	70	80	Not provided
				19-69	111	128	
Finland[3,4]	Dietary habits and nutrient intake of Finnish adolescents	2007	48hr dietary recall	14	77	82	Not provided
	FINDIET 2012	2012	48hr dietary recall	25-64	95	104	Vegetables 33-40%
				65-74	87	99	Fats (24-30%) Meat (8-12%)
Germany[5]	EsKiMo	2006	3-day diary	6	152	173	Not provided
				7-9	183	199	
				10-11	193	206	
				12	316	320	
				13-14	328	344	
				15-17	340	409	
Japan[6]	Kagwa University	2003	3-day diary	20-23	230.2		Pulses (45%)

[1] Moyersoen *et al.* (2017), [2] Buurma-Rethans and Van Rossum (2015) [3] Hoppu *et al.* (2010), [4] Helldán *et al.* (2013), [5] Mensink *et al.* (2007), [6] (Kamao *et al.*, 2007)

References

Anses/CIQUAL. 2013. *French food composition table version 2013* [Online]. Available: https://pro.anses.fr/TableCIQUAL/ [Accessed 2017].

Apalset, E., Gjesdal, C. G., Eide, G. E. & Tell, G. S. (2011). Intake of vitamin K1 and K2 and risk of hip fractures: The Hordaland Health Study. *Bone,* 49**,** 990-5.

Apalset, E. M., Gjesdal, C. G., Eide, G. E., Johansen, A.-M. W., Drevon, C. A. & Tell, G. S. (2010). Dietary vitamins K1, K2 and bone mineral density: the Hordaland Health Study. *Archives of Osteoporosis,* 5**,** 73-81.

Beulens, J. W., Bots, M. L., Atsma, F., Bartelink, M. L., Prokop, M., Geleijnse, J. M., Witteman, J. C., Grobbee, D. E. & van der Schouw, Y. T. (2009). High dietary menaquinone intake is associated with reduced coronary calcification. *Atherosclerosis,* 203**,** 489-93.

Beulens, J. W., van der, A. D., Grobbee, D. E., Sluijs, I., Spijkerman, A. M. & van der Schouw, Y. T. (2010). Dietary phylloquinone and menaquinones intakes and risk of type 2 diabetes. *Diabetes Care,* 33**,** 1699-705.

Binkley, N. C., Krueger, D. C., Engelke, J. A., Foley, A. L. & Suttie, J. W. (2000). Vitamin K supplementation reduces serum concentrations of under-gamma-carboxylated osteocalcin in healthy young and elderly adults. *American Journal of Clinical Nutrition,* 72**,** 1523-8.

Binkley, N. C., Krueger, D. C., Kawahara, T. N., Engelke, J. A., Chappell, R. J. & Suttie, J. W. (2002). A high phylloquinone intake is required to achieve maximal osteocalcin gamma-carboxylation. *American Journal of Clinical Nutrition,* 76**,** 1055-60.

Bolton-Smith, C., Price, R. J., Fenton, S. T., Harrington, D. J. & Shearer, M. J. (2000). Compilation of a provisional UK database for the phylloquinone (vitamin K1) content of foods. *British Journal of Nutrition,* 83**,** 389-99.

Booth, S. L. (2009). Roles for vitamin K beyond coagulation. *The Annual Review of Nutrition,* 29**,** 89-110.

Booth, S. L. & Al Rajabi, A. (2008). Determinants of vitamin K status in humans. *Vitamins and Hormones,* 78**,** 1-22.

Booth, S. L., Martini, L., Peterson, J. W., Saltzman, E., Dallal, G. E. & Wood, R. J. (2003). Dietary phylloquinone depletion and repletion in older women. *Journal of Nutrition,* 133**,** 2565-9.

Booth, S. L., O'Brien-Morse, M. E., Dallal, G. E., Davidson, K. W. & Gundberg, C. M. (1999). Response of vitamin K status to different intakes and sources of phylloquinone-rich foods: comparison of younger and older adults. *The American Journal of Clinical Nutrition,* 70**,** 368-377.

Booth, S. L., Sadowski, J. A., Weihrauch, J. L. & Ferland, G. (1993). Vitamin K1 (Phylloquinone) Content of Foods: A Provisional Table. *Journal of Food Composition and Analysis,* 6**,** 109-120.

Booth, S. L. & Suttie, J. W. (1998). Dietary intake and adequacy of vitamin K. *Journal of Nutrition,* 128**,** 785-8.

Booth, S. L., Tucker, K. L., McKeown, N. M., Davidson, K. W., Dallal, G. E. & Sadowski, J. A. (1997). Relationships between dietary intakes and fasting plasma concentrations of fat-soluble vitamins in humans. *Journal of Nutrition,* 127**,** 587-92.

Buurma-Rethans & Van Rossum. 2015. *Inname van vitamine K door kinderen en volwassenen in Nederland* [Online]. Available: https://www.rivm.nl/sites/default/files/2018-11/Inneming%20van%20vitamine%20K%20-%20versie%202.pdf [Accessed 2017].

Conly, J. M., Stein, K., Worobetz, L. & Rutledge-Harding, S. (1994). The contribution of vitamin K2 (menaquinones) produced by the intestinal microflora to human nutritional requirements for vitamin K. *American Journal of Gastroenterology,* 89**,** 915-23.

Dalmeijer, G. W., van der Schouw, Y. T., Magdeleyns, E., Ahmed, N., Vermeer, C. & Beulens, J. W. (2012). The effect of menaquinone-7 supplementation on circulating species of matrix Gla protein. *Atherosclerosis,* 225**,** 397-402.

Davidson, R. T., Foley, A. L., Engelke, J. A. & Suttie, J. W. (1998). Conversion of Dietary Phylloquinone to Tissue Menaquinone-4 in Rats is Not Dependent on Gut Bacteria. *The Journal of Nutrition,* 128**,** 220-223.

Department of Health (1991). *Dietary Reference Values for food energy and nutrients for the United Kingdom.* HMSO, London, UK.

Deutsche Gesellschaft fur Ernahrung (2012). *Ernahrungsbericht 2012.* Bonn, Germany.

Dialameh, G. H., Taggart, W. V., Matschiner, J. T. & Olson, R. E. (1971). Isolation and characterization of menaquinone-4 as a product of menadione metabolism in chicks and rats. *International Journal for Vitamin and Nutrition Research,* 41**,** 391-400.

Dismore, M. L., Haytowitz, D. B., Gebhardt, S. E., Peterson, J. W. & Booth, S. L. (2003). Vitamin K content of nuts and fruits in the US diet. *Journal of the American Dietetic Association,* 103**,** 1650-2.

Duggan, P., Cashman, K. D., Flynn, A., Bolton-Smith, C. & Kiely, M. (2004). Phylloquinone (vitamin K1) intakes and food sources in 18-64-year-old Irish adults. *British Journal of Nutrition,* 92**,** 151-8.

Dumont, J. F., Peterson, J., Haytowitz, D. & Booth, S. L. (2003). Phylloquinone and dihydrophylloquinone contents of mixed dishes, processed meats, soups and cheeses. *Journal of Food Composition and Analysis,* 16**,** 595-603.

Dutch Nutrients Database (NEVO). 2016. Available: https://www.rivm.nl/en/dutch-food-composition-database [Accessed 2017].

EFSA NDA Panel (2017). Dietary reference values for Vitamin K. *EFSA Journal,* 15.

EFSA Panel on Additives and Products or Substances used in Animal Feed (2014). Scientific Opinion on the safety and efficacy of vitamin K3 (menadione sodium bisulphite and menadione nicotinamide bisulphite) as a feed additive for all animal species. *EFSA Journal,* 12**,** 3532.

EFSA Panel on Dietetic Products, N., Allergies, Turck, D., Bresson, J.-L., Burlingame, B., Dean, T., Fairweather-Tait, S., Heinonen, M., Hirsch-Ernst, K. I., Mangelsdorf, I., McArdle, H. J., Naska, A., Nowicka, G., Pentieva, K., Sanz, Y., Siani, A., Sjödin, A., Stern, M., Tomé, D., Van Loveren, H., Vinceti, M., Willatts, P., Lamberg-Allardt, C., Przyrembel, H., Tetens, I., Dumas, C., Fabiani, L., Ioannidou, S. & Neuhäuser-Berthold, M. (2017). Dietary reference values for vitamin K. *EFSA Journal,* 15**,** e04780.

Elder, S. J., Haytowitz, D. B., Howe, J., Peterson, J. W. & Booth, S. L. (2006). Vitamin k contents of meat, dairy, and fast food in the u.s. Diet. *Journal of Agricultural and Food Chemistry,* 54**,** 463-7.

Elmadfa, I., Hasenegger, V., Wagner, K., Putz, P., Weidl, N.-M., Wottawa, D., Kuen, T., Seiringer, G., Meyer, A., Sturtzel, B., Kiefer, I., Zilberszac, A., Sgarabottolo, V., Meidlinger, B. & Rieder, A. (2012). Österreichischer Ernährungsbericht 2012.

Elmadfa, I. & Meyer, A. L. (2010). Importance of food composition data to nutrition and public health. *European Journal of Clinical Nutrition,* 64 Suppl 3**,** S4-7.

Ferland, G. & Sadowski, J. A. (1992a). Vitamin K1 (phylloquinone) content of edible oils: effects of heating and light exposure. *Journal of Agricultural and Food Chemistry,* 40**,** 1869-1873.

Ferland, G. & Sadowski, J. A. (1992b). Vitamin K1 (phylloquinone) content of green vegetables: effects of plant maturation and geographical growth location. *Journal of Agricultural and Food Chemistry,* 40**,** 1874-1877.

Ferland, G., Sadowski, J. A. & O'Brien, M. E. (1993). Dietary induced subclinical vitamin K deficiency in normal human subjects. *The Journal of clinical investigation,* 91**,** 1761-1768.

Ferreira, D. W. (2006). Vitamin K Contents of Grains, Cereals, Fast-Food Breakfasts, and Baked Goods. *Journal of Food Science,* 71**,** S66-S70.

Finnan, E. G., Harshman, S. G., Haytowitz, D. B. & Booth, S. L. (2017). Mixed dishes are an unexpected source of dietary vitamin K. *Journal of Food Composition and Analysis,* 64**,** 127-131.

Finnish National Food Composition Database. 2019. *National Institute for Health and Welfare.* [Online]. Available: https://fineli.fi/fineli/en/index [Accessed 2017].

Food Composition Database Italy (BDA). 2015. *European Institute of Oncology 2015* [Online]. Available: http://www.bda-ieo.it/ [Accessed 2017].

Fu, X., Harshman, S. G., Shen, X., Haytowitz, D. B., Karl, J. P., Wolfe, B. E. & Booth, S. L. (2017). Multiple Vitamin K Forms Exist in Dairy Foods. *Current Developments in Nutrition,* 1**,** e000638-e000638.

Fu, X., Shen, X., Finnan, E. G., Haytowitz, D. B. & Booth, S. L. (2016). Measurement of Multiple Vitamin K Forms in Processed and Fresh-Cut Pork Products in the U.S. Food Supply. *Journal of Agricultural and Food Chemistry,* 64**,** 4531-5.

Garber, A. K., Binkley, N. C., Krueger, D. C. & Suttie, J. W. (1999). Comparison of phylloquinone bioavailability from food sources or a supplement in human subjects. *Journal of Nutrition,* 129**,** 1201-3.

Gast, G. C., de Roos, N. M., Sluijs, I., Bots, M. L., Beulens, J. W., Geleijnse, J. M., Witteman, J. C., Grobbee, D. E., Peeters, P. H. & van der Schouw, Y. T. (2009). A high menaquinone intake reduces the incidence of coronary heart disease. *Nutrition, Metabolism, and Cardiovascular Diseases,* 19**,** 504-10.

Geleijnse, J. M., Grobbee, D. E., Pols, H. A. P., Hofman, A., Witteman, J. C. M. & Vermeer, C. (1999). Nutritional Intake of Vitamins K1 (Phylloquinone) and K2 (Menaquinone) in The Netherlands AU - Schurgers, L. J. *Journal of Nutritional & Environmental Medicine,* 9**,** 115-122.

Geleijnse, J. M., Vermeer, C., Grobbee, D. E., Schurgers, L. J., Knapen, M. H., van der Meer, I. M., Hofman, A. & Witteman, J. C. (2004). Dietary intake of menaquinone is associated with a reduced risk of coronary heart disease: the Rotterdam Study. *Journal of Nutrition,* 134**,** 3100-5.

German Food Code and Nutrient Database. 2017. *Bundeslebensmittelschlüssel version 3.02* [Online]. Max Rubner Institut. Available: https://www.blsdb.de/ [Accessed 2017].

Gijsbers, B. L., Jie, K. S. & Vermeer, C. (1996). Effect of food composition on vitamin K absorption in human volunteers. *British Journal of Nutrition,* 76**,** 223-9.

Gross, J., Cho, W. K., Lezhneva, L., Falk, J., Krupinska, K., Shinozaki, K., Seki, M., Herrmann, R. G. & Meurer, J. (2006). A plant locus essential for phylloquinone (vitamin K1) biosynthesis originated from a fusion of four eubacterial genes. *Journal of Biological Chemistry,* 281**,** 17189-96.

Halder, M., Petsophonsakul, P., Akbulut, A. C., Pavlic, A., Bohan, F., Anderson, E., Maresz, K., Kramann, R. & Schurgers, L. (2019). Vitamin K: Double Bonds beyond Coagulation Insights into Differences between Vitamin K1 and K2 in Health and Disease. *International Journal of Molecular Sciences,* 20**,** 896.

Hannon, E. M., Cashman, K., Kiely, M. & Flynn, A. (2007). Phylloquinone intakes and food sources in Irish children aged 5-12 years. *Proceedings of the Nutrition Society,* 66**,** 32A-114A.

Hayes, A., Hennessy, A., Walton, J., McNulty, B. A., Lucey, A. J., Kiely, M., Flynn, A. & Cashman, K. D. (2016). Phylloquinone Intakes and Food Sources and

Vitamin K Status in a Nationally Representative Sample of Irish Adults. *Journal of Nutrition,* 146**,** 2274-2280.

Helldán, A., Raulio S, Kosola M, Tapanainen H, Ovaskainen ML & S, V. (2013). Finravinto 2012-tutkimus-The National FINDIET 2012 Survey. *Raportti: 2013_016,* Raportti, Helsinki.

Hoppu, U., Lehtisalo, J., Tapanainen, H. & Pietinen, P. (2010). Dietary habits and nutrient intake of Finnish adolescents. *Public Health Nutrition,* 13**,** 965-72.

Institute of Medicine (2001). *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc.* Washington (DC): National Academies Press (US).

Kamao, M., Suhara, Y., Tsugawa, N., Uwano, M., Yamaguchi, N., Uenishi, K., Ishida, H., Sasaki, S. & Okano, T. (2007). Vitamin K content of foods and dietary vitamin K intake in Japanese young women. *Journal of Nutritional Science and Vitaminology,* 53**,** 464-70.

Karl, J. P., Meydani, M., Barnett, J. B., Vanegas, S. M., Barger, K., Fu, X., Goldin, B., Kane, A., Rasmussen, H., Vangay, P., Knights, D., Jonnalagadda, S. S., Saltzman, E., Roberts, S. B., Meydani, S. N. & Booth, S. L. (2017). Fecal concentrations of bacterially derived vitamin K forms are associated with gut microbiota composition but not plasma or fecal cytokine concentrations in healthy adults. *American Journal of Clinical Nutrition,* 106**,** 1052-1061.

Kim, M.-S., Kim, E.-S. & Sohn, C.-M. (2015). Dietary intake of vitamin K in relation to bone mineral density in Korea adults: The Korea National Health and Nutrition Examination Survey (2010-2011). *Journal of Clinical Biochemistry and Nutrition,* 57**,** 223-227.

Knapen, M. H., Braam, L. A., Drummen, N. E., Bekers, O., Hoeks, A. P. & Vermeer, C. (2015). Menaquinone-7 supplementation improves arterial stiffness in healthy postmenopausal women. A double-blind randomised clinical trial. *Thrombosis and Haemostasis,* 113**,** 1135-44.

Knapen, M. H., Drummen, N. E., Smit, E., Vermeer, C. & Theuwissen, E. (2013). Three-year low-dose menaquinone-7 supplementation helps decrease bone loss in healthy postmenopausal women. *Osteoporosis International,* 24**,** 2499-507.

Koivu-Tikkanen, T. J., Ollilainen, V. & Piironen, V. I. (2000). Determination of phylloquinone and menaquinones in animal products with fluorescence detection after postcolumn reduction with metallic zinc. *Journal of Agricultural and Food Chemistry,* 48**,** 6325-31.

Manios, Y., Grammatikaki, E., Papoutsou, S., Liarigkovinos, T., Kondaki, K. & Moschonis, G. (2008). Nutrient intakes of toddlers and preschoolers in Greece: the GENESIS study. *Journal of the American Dietetic Association,* 108**,** 357-61.

Manoury, E., Jourdon, K., Boyaval, P. & Fourcassie, P. (2013). Quantitative measurement of vitamin K2 (menaquinones) in various fermented dairy products using a reliable high-performance liquid chromatography method. *Journal of Dairy Science,* 96**,** 1335-46.

McCann, J. C. & Ames, B. N. (2009). Vitamin K, an example of triage theory: is micronutrient inadequacy linked to diseases of aging? *American Journal of Clinical Nutrition,* 90**,** 889-907.

Mensink, G. B., Bauch, A., Vohmann, C., Stahl, A., Six, J., Kohler, S., Fischer, J. & Heseker, H. (2007). [EsKiMo - the nutrition module in the German Health Interview and Examination Survey for Children and Adolescents (KiGGS)]. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz,* 50**,** 902-8.

Moyersoen, I., Devleesschauwer, B., Dekkers, A., de Ridder, K., Tafforeau, J., van Camp, J., van Oyen, H. & Lachat, C. (2017). Intake of Fat-Soluble Vitamins in the Belgian Population: Adequacy and Contribution of Foods, Fortified Foods and Supplements. *Nutrients,* 9.

Nimptsch, K., Rohrmann, S., Kaaks, R. & Linseisen, J. (2010). Dietary vitamin K intake in relation to cancer incidence and mortality: results from the Heidelberg cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC-Heidelberg). *American Journal of Clinical Nutrition,* 91**,** 1348-58.

Nimptsch, K., Rohrmann, S. & Linseisen, J. (2008). Dietary intake of vitamin K and risk of prostate cancer in the Heidelberg cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC-Heidelberg). *American Journal of Clinical Nutrition,* 87**,** 985-92.

Nordic Council of Ministers 2014. *Nordic Nutrition Recommendations 2012 : Integrating nutrition and physical activity,* Copenhagen, Nordisk Ministerråd.

O'Connor, E., Molgaard, C., Michaelsen, K. F., Jakobsen, J., Lamberg-Allardt, C. J. & Cashman, K. D. (2007). Serum percentage undercarboxylated osteocalcin, a sensitive measure of vitamin K status, and its relationship to bone health indices in Danish girls. *British Journal of Nutrition,* 97**,** 661-6.

Okano, T., Shimomura, Y., Yamane, M., Suhara, Y., Kamao, M., Sugiura, M. & Nakagawa, K. (2008). Conversion of phylloquinone (Vitamin K1) into menaquinone-4 (Vitamin K2) in mice: two possible routes for menaquinone-4 accumulation in cerebra of mice. *Journal of Biological Chemistry,* 283**,** 11270-9.

Ortega Anta, R. M., Gonzalez-Rodriguez, L. G., Navia Lomban, B. & Lopez-Sobaler, A. M. (2014). Vitamin K adequacy ina representative sample of Spanish adults. Dietary determinants. *Nutricion Hospitalaria,* 29**,** 187-95.

Peterson, J. W., Muzzey, K. L., Haytowitz, D., Exler, J., Lemar, L. & Booth, S. L. (2002). Phylloquinone (vitamin K1) and dihydrophylloquinone content of fats and oils. *Journal of the American Oil Chemists' Society,* 79**,** 641-646.

Popko, J., Karpinski, M., Chojnowska, S., Maresz, K., Milewski, R., Badmaev, V. & Schurgers, L. J. (2018). Decreased Levels of Circulating Carboxylated Osteocalcin in Children with Low Energy Fractures: A Pilot Study. *Nutrients,* 10.

Presse, N., Potvin, S., Bertrand, B., Calvo, M. S. & Ferland, G. (2015). Phylloquinone content of herbs, spices and seasonings. *Journal of Food Composition and Analysis,* 41**,** 15-20.

Prynne, C. J., Thane, C. W., Prentice, A. & Wadsworth, M. E. (2005). Intake and sources of phylloquinone (vitamin K(1)) in 4-year-old British children: comparison between 1950 and the 1990s. *Public Health Nutrition,* 8**,** 171-80.

Public Health England Composition of Foods Integrated Dataset. 2015. *McCance and Widdowson's The Composition of Foods Integrated Dataset 2015* [Online]. Available: https://www.gov.uk/government/publications/composition-of-foods-integrated-dataset-cofid.

Sato, T., Schurgers, L. J. & Uenishi, K. (2012). Comparison of menaquinone-4 and menaquinone-7 bioavailability in healthy women. *Nutrition Journal,* 11**,** 93.

Schurgers, L. J., Teunissen, K. J., Hamulyak, K., Knapen, M. H., Vik, H. & Vermeer, C. (2007). Vitamin K-containing dietary supplements: comparison of synthetic vitamin K1 and natto-derived menaquinone-7. *Blood,* 109**,** 3279-83.

Schurgers, L. J. & Vermeer, C. (2000). Determination of phylloquinone and menaquinones in food. Effect of food matrix on circulating vitamin K concentrations. *Haemostasis,* 30**,** 298-307.

Shea, M. K. & Booth, S. L. (2016). Concepts and Controversies in Evaluating Vitamin K Status in Population-Based Studies. *Nutrients,* 8.

Shearer, M. J. (1995). Vitamin K. *The Lancet,* 345**,** 229-234.

Shearer, M. J. & Bolton-Smith, C. (2000). The UK food data-base for vitamin K and why we need it. *Food Chemistry,* 68**,** 213-218.

Shearer, M. J. & Newman, P. (2008). Metabolism and cell biology of vitamin K. *Thrombosis and Haemostasis,* 100**,** 530-47.

Simes, D. C., Viegas, C. S. B., Araujo, N. & Marreiros, C. (2020). Vitamin K as a Diet Supplement with Impact in Human Health: Current Evidence in Age-Related Diseases. *Nutrients,* 12.

Sokoll, L. J., Booth, S. L., O'Brien, M. E., Davidson, K. W., Tsaioun, K. I. & Sadowski, J. A. (1997). Changes in serum osteocalcin, plasma phylloquinone, and urinary gamma-carboxyglutamic acid in response to altered intakes of dietary phylloquinone in human subjects. *American Journal of Clinical Nutrition,* 65**,** 779-84.

Stafford, D. W. (2005). The vitamin K cycle. *Journal of Thrombosis and Haemostasis,* 3**,** 1873-8.

Suttie, J. W. (1992). Vitamin K and human nutrition. *Journal of the American Dietetic Association,* 92**,** 585-90.

Suttie, J. W. (1995). The importance of menaquinones in human nutrition. *Annual Review of Nutrition,* 15**,** 399-417.

Swedish National Food Database. 2017. *National Food Administration Sweden* [Online]. Available: https://www.livsmedelsverket.se/om-oss [Accessed 2017].

Tarvainen, M., Fabritius, M. & Yang, B. (2019). Determination of vitamin K composition of fermented food. *Food Chemistry,* 275**,** 515-522.

Technical University of Denmark. 2007. *The official Danish Food Composition Database* [Online]. Available: http://www.foodcomp.dk/v7/fcdb_default.asp [Accessed January 2016].

Thane, C. W., Bates, C. J., Shearer, M. J., Unadkat, N., Harrington, D. J., Paul, A. A., Prentice, A. & Bolton-Smith, C. (2002a). Plasma phylloquinone (vitamin K1) concentration and its relationship to intake in a national sample of British elderly people. *British Journal of Nutrition,* 87**,** 615-22.

Thane, C. W., Bolton-Smith, C. & Coward, W. A. (2006a). Comparative dietary intake and sources of phylloquinone (vitamin K1) among British adults in 1986-7 and 2000-1. *British Journal of Nutrition,* 96**,** 1105-15.

Thane, C. W., Paul, A. A., Bates, C. J., Bolton-Smith, C., Prentice, A. & Shearer, M. J. (2002b). Intake and sources of phylloquinone (vitamin K1): variation with socio-demographic and lifestyle factors in a national sample of British elderly people. *British Journal of Nutrition,* 87**,** 605-13.

Thane, C. W., Wang, L. Y. & Coward, W. A. (2006b). Plasma phylloquinone (vitamin K1) concentration and its relationship to intake in British adults aged 19-64 years. *British Journal of Nutrition,* 96**,** 1116-24.

Theuwissen, E., Cranenburg, E. C., Knapen, M. H., Magdeleyns, E. J., Teunissen, K. J., Schurgers, L. J., Smit, E. & Vermeer, C. (2012). Low-dose menaquinone-7 supplementation improved extra-hepatic vitamin K status, but had no effect on thrombin generation in healthy subjects. *British Journal of Nutrition,* 108**,** 1652-7.

Thijssen, H. H., Vervoort, L. M., Schurgers, L. J. & Shearer, M. J. (2006). Menadione is a metabolite of oral vitamin K. *British Journal of Nutrition,* 95.

TürKomp Turkish Food Composition Database. 2014. Available: http://turkomp.gov.tr/database?type=foods [Accessed 2017].

US Department of Agriculture (2018). Nutrient Intakes from Food and Beverages: Mean amounts consumed per Individual , by Gender and Age, What we eat in America, NHANES 2015-2016.

USDA National Nutrient Database for Standard References Release 28. 2015. Washington (DC): USDA Agricultural Research Service. Available: http://www.ars.usda.gov/nutrientdata [Accessed January 2016].

Van Summeren, M., Braam, L., Noirt, F., Kuis, W. & Vermeer, C. (2007). Pronounced elevation of undercarboxylated osteocalcin in healthy children. *Pediatric Research,* 61**,** 366-70.

Van Summeren, M. J. H., Braam, L. A. J. L. M., Lilien, M. R., Schurgers, L. J., Kuis, W. & Vermeer, C. (2009). The effect of menaquinone-7 (vitamin K2) supplementation on osteocalcin carboxylation in healthy prepubertal children. *British Journal of Nutrition,* 102**,** 1171-1178.

Vermeer, C. (2012). Vitamin K: the effect on health beyond coagulation – an overview. *Food & Nutrition Research,* 56**,** 10.3402/fnr.v56i0.5329.

Vermeer, C., Raes, J., van 't Hoofd, C., Knapen, M. H. J. & Xanthoulea, S. (2018). Menaquinone Content of Cheese. *Nutrients,* 10.

Vissers, L. E., Dalmeijer, G. W., Boer, J. M., Monique Verschuren, W. M., van der Schouw, Y. T. & Beulens, J. W. (2013). Intake of dietary phylloquinone and menaquinones and risk of stroke. *J Am Heart Assoc,* 2**,** e000455.

Walther, B., Karl, J. P., Booth, S. L. & Boyaval, P. (2013). Menaquinones, bacteria, and the food supply: the relevance of dairy and fermented food products to vitamin K requirements. *Advances in Nutrition,* 4**,** 463-73.

WHO/FAO (2004). *Vitamin and mineral requirements in human nutrition: report of a joint FAO/WHO expert consultation.* Bankok, Thailand.

Williams, C. (2005). *The Different Uses of Food Composition Databases.* https://www.bezpecnostpotravin.cz/UserFiles/File/Kvasnickova2/EuroFIR_2.pdf.

Zwakenberg, S. R., den Braver, N. R., Engelen, A. I. P., Feskens, E. J. M., Vermeer, C., Boer, J. M. A., Verschuren, W. M. M., van der Schouw, Y. T. & Beulens, J. W. J. (2017). Vitamin K intake and all-cause and cause specific mortality. *Clinical Nutrition,* 36**,** 1294-1300.

Aims and objectives

The overall aim of this thesis was to estimate the intake, adequacy and dietary sources of vitamin K_1 and vitamin K_2 in nationally representative samples of the Irish population aged 1-90 years and to examine any changes in vitamin K_1 or vitamin K_2 intakes and sources in school-aged children between 2003-04 and 2017-18. To facilitate this research, a key aim of this thesis was to update the Irish Food Composition Database (IFCD) with composition data for vitamin K_1 and vitamin K_2. This research used data from five national dietary surveys carried out by the Irish Universities Nutrition Alliance (www.iuna.net) over the last 20 years. These surveys included the National Children's Food Survey (5-12y) (2003-04), the National Teens' Food Survey (13-17y) (2005-06), the National Adult Nutrition Survey (18-90y) (2008-10), the National Pre-school Nutrition Survey (1-4y) (2010-11) and the National Children's Food Survey II (5-12y) (2017-18).

Objectives:

1. To update the Irish Food Composition Database with composition data for vitamin K_1 and vitamin K_2.
2. To estimate the intake, adequacy and sources of vitamin K_1 (phylloquinone) in Irish children aged 1-17 years.
3. To estimate the intake and sources of vitamin K_2 (menaquinones) in the Irish population aged 1-90 years.
4. To investigate changes in vitamin K_1 and vitamin K_2 intakes and sources in Irish school children aged 5-12 years between 2003-04 and 2017-18.

Chapter 2

Methodology of the Irish National Dietary Surveys

Methodology

Analyses for the present study were based on data from five nationally representative dietary surveys of the Irish population; this chapter outlines the methodology for each of these surveys. The five surveys include: the National Children's Food Survey (NCFS) of 5-12 year olds (2003-04), the National Teens' Food Survey (NTFS) of 13-17 year olds (2005-06), the National Adult Nutrition Survey (NANS) of 18-90 year olds (2008-10), the National Pre-school Nutrition Survey (NPNS) of 1-4 year olds (2010-11) and the National Children's Food Survey II of 5-12 year olds (NCFS II) (2017-19) (www.iuna.net). Each survey was a cross sectional study carried out by the nutrition centres in University College Cork, Cork Institute of Technology, University College Dublin and Technological University Dublin, which form part of the Irish Universities Nutrition Alliance (IUNA). Methods relevant to this thesis are outlined below with further information available on www.iuna.net.

Ethical approval

All surveys were conducted in accordance with guidelines laid down in the Declaration of Helsinki. Ethical approval for each survey was obtained from either St. James' Hospital and Federated Dublin Voluntary Hospitals Joint Research Ethics Committee (NCFS) or the University College Cork Clinical Research Ethics Committee of the Cork Teaching Hospitals (NTFS, NANS, NPNS & NCFS II).

Written informed consent was obtained from all participants and/or parents/guardians before commencement of each survey.

Sampling and recruitment methodology

National Children's Food Survey II (2017-18) and the National Children's Food Survey (2003-04)

The NCFS II and the NCFS had the same method of sampling and recruitment which is summarised as follows; 600 children (300 boys, 300 girls) and 594 children (293 boys, 301 girls) aged 5 to 12 years from across the Republic of Ireland took part in the NCFS II (from April 2017 to May 2018) and in the NCFS (from March 2003 to March 2004), respectively. For both surveys, a database of primary schools in Ireland (provided by the Department of Education and Skills) was used to select schools to provide a demographically balanced sample with respect to urban/rural location and socio-economic grouping. The principals of selected schools in the NCFS II and the NCFS were contacted, with 80% and 90% of those contacted agreeing to take part in the study, respectively. Parents/guardians of children who were randomly selected from the school roll were contacted with information on the survey and participation was invited. Children who returned a reply slip were excluded if they were not between the ages of 5 and 12 years, if they belonged to an age or sex or urban/rural location for which the appropriate number of children had already been recruited or if another member of their household had already been recruited for participation in the survey. Where families opted in, a researcher visited the home to explain the survey in more detail and to obtain consent from both parents/guardians and the child. The overall response rate for the NCFS II and the NCFS was 65% and 66%, respectively. Demographic analysis of the NCFS II and NCFS showed it to be representative of children in Ireland with respect to age, gender and urban/rural location when compared to Census 2016 and Census 2002 data, respectively (Central Statistics Office, 2003, Central Statistics Office, 2017). However, the NCFS II sample contained a higher proportion of children of professional workers and a lower proportion of children of semi-skilled and unskilled workers than the national population and all data in this thesis have been weighted to account for these differences.

National Teens Food Survey (2005-06)

A sample of 441 teenagers (224 boys, 217 girls) aged 13 to 17 years from across the Republic of Ireland took part in the NTFS from September 2005 to September 2006. Schools were selected from a database of secondary schools available from the Department of Education and Science. A number of schools were randomly selected to provide a demographically balanced sample with respect to urban/rural location and socio-economic grouping. All urban schools selected were located in Cork or Dublin and all rural schools were located outside of Cork and Dublin. The principals of selected schools were contacted, with 95% of those contacted agreeing to take part in the study. Parents/guardians of teenagers who were randomly selected from the school roll were contacted with information on the survey and participation was invited. Teenagers who returned a reply slip were excluded if they were not between the ages of 13 and 17 years, if they belonged to an age or sex or urban/rural location for which the appropriate number of teenagers had already been recruited or if another member of their household had already been recruited for participation in the survey. Where families opted in, a researcher visited the home to explain the survey in more detail and to obtain consent from both parents/guardians and the teenager. The overall response rate was 63%. Analysis of the demographic features in this sample has shown it to be a representative sample of the Irish teenagers with respect to age, sex, social class, socio-economic group and urban/rural location when compared to the Census 2002 data (Central Statistics Office, 2003).

National Adult Nutrition Survey (2008-10)

A sample of 1500 adults (740 males, 760 females) aged 18 to 90 years from across the Republic of Ireland took part in the NANS from October 2008 to April 2010. Eligible participants were adults aged 18 years and over who were free-living and who were not pregnant or breast-feeding. A sample of adults were randomly selected from a database of names and addresses held by Data Ireland (An Post). An introductory letter and information leaflet were posted to each person selected from the database. A researcher called to potential participants' homes to introduce the survey and invite participation. If the individual agreed to take part, a consent form was signed and the survey commenced. If the person was not at home, the researcher called on three more occasions on different days and at different times, before deeming them ineligible. A second level of recruitment was carried out for groups that were not highly represented in the sample, particularly 18-35 year olds. Names and addresses were compiled for this through referrals from previous participants. The final response rate for the survey was 60%. Demographic analysis of the sample has shown it to be nationally representative of Irish adults with respect to age, gender, social class and urban/rural location when compared to the Census 2006 data (Central Statistics Office, 2007).

National Pre-School Nutrition Survey (2010-11)

A sample of 500 children (boys 251, girls 249), aged from 12 months to 59 months inclusive, from across the Republic of Ireland took part in the NPNS between October 2010 and September 2011. Individuals were selected for participation from a database of names and addresses compiled by 'eumom' (an Irish parenting resource (www.eumom.ie) or from randomly chosen childcare facilities in select locations. An introductory information letter and brochure were sent to the parent/guardian of the individuals selected. In all cases, the onus was on the prospective participant to 'opt in'. For those participants that 'opted in' a researcher called to their home in the following days to further explain the survey. Eligible children (aged from 12 to 59 months inclusive, who had not yet started primary school) were invited to participate and a consent form was signed by their parent/guardian. Demographic analysis of the sample has shown it to be representative of young children in Ireland with respect to age, gender, and urban/rural location when compared to Census 2006 data (Central Statistics Office, 2007). The sample was also generally representative of social class, although there were a higher proportion of children of professional workers. However, as there were no significant differences between social classes for food and nutrient intakes or body weight the data have not been adjusted for this (Irish Universities Nutrition Alliance (IUNA) (2012)).

Dietary data collection

An overview of the methods of dietary data collection is presented in **Table 1.** For the NCFS, 594 children aged 5-12 years completed a 7-day weighed food record with a total of four visits from the fieldworker over the recording period. Similarly, 441 teenagers aged 13-17 years completed the NTFS using a 7-day semi-weighed food record with four visits from the fieldworker over the recording period. Fifteen hundred adults aged 18-90 years participated in the NANS, which collected dietary data using a 4-day semi weighed food record. Each participant was visited 3 times over the recording period by the trained researcher. Food and beverage intake data were estimated for 500 pre-school children aged 1-4 years in the NPNS using a 4-day weighed food record. The NCFS II collected dietary data from 600 children aged 5-12 years using a 4-day weighed food diary. The fieldworker visited each participant 3 times over the recording period for both the NPNS and the NCFS II; a training visit to demonstrate how to keep the food diary and use the weighing scales, a second visit 24-36 hours into the recording period to review the diary, check for completeness, and clarify details regarding specific food descriptors and quantities, and a final visit one or two days after the recording period to review the remaining recording days and to collect the diary.

For each survey, detailed information was collected for all foods, beverages and nutritional supplements (at brand level) relating to the amount, type, and cooking method (if applicable). Leftovers were also accounted for and details of recipes of composite dishes were collected over the recording period. Data were collected on the time of each eating or drinking occasion, the participant's definition of each eating or drinking occasion (e.g. breakfast, morning snack, lunch) and the location of the preparation of the meal or snack consumed (e.g. home, work, school).

Food quantification and coding

A quantification protocol that was established by the IUNA for the North/South Ireland Food Consumption Survey (NSIFCS) (Harrington *et al.*, 2001) was adapted for each survey. This protocol is summarised as follows and the percentage of each quantification method used in each survey is outlined in **table 1:**

1) Weighed (using the digital food scales provided to each participant) or manufacturers' information on product labels
2) Age appropriate photographic food atlas (Nelson M *et al.*, 1997, Foster *et al.*, 2010)
3) Standard portion weights (Food Standards Agency, 2002a, Lyons *et al.*, 2013)
4) Household measures
5) Estimated based on the researchers knowledge of the participants previous eating patterns (only used when no other quantification method was appropriate)

Dietary data entry

Every food and beverage consumed in each survey was assigned a unique food code depending on its nutritional profile and brand information allowing the inclusion of recipes of composite dishes, nutritional supplements, fortified foods and generic Irish foods that were commonly consumed and were updated for each survey.

For all of the surveys, dietary data were entered into either the data entry system WISP© (Tinuviel Software, Anglesey, UK) (for the NCFS, NTFS, NANS and the NPNS) or Nutritics© (for the NCFS II). Both WISP© and Nutritics© estimate nutrient intakes using UK food composition data from McCance & Widdowson's The Composition of Foods, Seventh (Food Standards Agency, 2015), sixth (Food Standards Agency, 2002b) and fifth (Holland *et al.*, 1995) editions plus all nine supplemental volumes (Holland *et al.*, 1988, Holland *et al.*, 1989, Holland *et al.*, 1991, Holland *et al.*, 1992a, Holland *et al.*, 1992b, Holland *et al.*, 1993, Chan *et al.*, 1994, Chan *et al.*, 1995, Chan *et al.*, 1996). A total of 1945, 1761, 2552, 1652 and 2046 food codes were included in the NCFS, NTFS, NANS, NPNS and NCFS II databases, respectively.

Quality control

Across all surveys, a number of quality procedures were put in place in an attempt to minimise error and ensure consistency throughout the collection and data entry of food intake. Researchers received training that included role-play workshops prior to commencing fieldwork, where they were trained to take a natural and friendly approach to fieldwork and to avoid prompting foods. This was carried out in an attempt to make participants feel at ease and so that the most reliable data possible could be obtained. It was stressed to participants that they should not try to change or improve their diet during the recording period.

Each fieldworker was primarily responsible for the collection, quantification, coding and data entry of their own participants' food diaries in an attempt to maintain consistency. Once the data entry was completed by the fieldworker, all diaries were re-checked and a percentage of diaries were re-checked by a different fieldworker. The survey co-ordinater then exported all diaries to either WISP© (NCFS, NTFS, NANS & NPNS) or Nutritics© (NCFS II) where a further quality control took place. All food codes and corresponding brand codes were compared to ensure no mismatches occurred. The consolidated data for each survey was then exported to SPSS and each variable exported was quality controlled for errors and outliers.

Databases

The NCFS, NTFS, NANS, NPNS and the NCFS II database comprises over 72,000, 46,470, 133,050, 36,000 and 41,780 rows of data, respectively, that describe every food and drink item consumed by each of the participants, at every eating occasion, for each of the recording days. For each item consumed, each database contains the actual day of the week, the definition of the eating occasion, where the meal was prepared, the time and location of consumption, the weight of food/drink consumed, brand description, packaging type and size and nutritional composition for a number of nutrients that are available in the UK composition of foods.

All food and drink items were allocated into one of the nineteen food groups (Appendix I) and then further subdivided into sixty-eight (NCFS, NTFS, NANS & NCFS II) or seventy-seven sub groups (NPNS) (Appendix II).

Anthropometric data

The Adequate Intake (AI) for vitamin K_1 is derived based on kilogram of body weight (μg/kg/d) (EFSA Panel on Dietetic Products *et al.*, 2017). For each survey, body weight was measured by the researcher in the participants' homes in duplicate using either a Seca 770 digital personal weighing scale (Chasmores Ltd, UK) (NCFS and NTFS), Seca Scales 385 (AccuScience, Ireland) (NPNS) or a Tanita body composition BC-420MA (Tanita Ltd, GB) (NANS and NCFS II) to the nearest 0.1kg. Participants were weighed after having voided, wearing light clothes and without shoes.

Table 1. Overview of each survey methodology and percentage (%) of each quantification method used to quantify foods consumed by participants of each survey

	NCFS (2003-04)	**NTFS (2005-06)**	**NANS (2008-10)**	**NPNS (2010-11)**	**NCFS II (2017-18)**
Number of participants	594	441	1500	500	600
Age group (years)	5-12	13-17	18-90	1-4	5-12
Length of data collection (days)	7	7	4	4	4
Number of visits from the researcher	4	4	3	3	3
Quantification method	Weighed	Semi-weighed	Semi-weighed	Weighed	Weighed
of which (%)					
Weighed by participant or manufacturer	*85*	*45*	*56*	*85*	*87*
Food Atlas[1]	*5*	*28*	*16*	*6*	*7*
Food Portion Sizes[2]	*4*	*10*	*11*	*1*	*3*
Irish Food Portion Size Database[3]	*1*	*8*	*4*	*0.5*	-
Household Measures	*2*	*7*	*11*	*6*	*1*
Estimated	*3*	*2*	*2*	*1.5*	*2*
Total	**100**	**100**	**100**	**100**	**100**

[1] Nelson M *et al.* (1997), Foster E *et al.* (2010)

[2] Food Standards Agency (2002a)

[3] Lyons *et al.* (2013)

References

Central Statistics Office (2003). *Census 2002 Principal Demographic Results.* Dublin: Central Statistics Office (CSO).

Central Statistics Office (2007). *Census 2006 Principal Demographic Results.* Dublin: Central Statistics Office (CSO).

Central Statistics Office (2017). *Census 2016 Summary Results.* Dublin: Central Statistics Office (CSO).

Chan, W., Brown, J., Church, S. M. & Buss, D. H. (1994). Miscellaneous Foods. Fourth Supplement to McCance & Widdowson's The Composition of Foods, 5th ed. Royal Society of Chemistry and Ministry of Agriculture, Fisheries and Food, London: HMSO.

Chan, W., Brown, J., Church, S. M. & Buss, D. H. (1995). Meat Poultry and Game. Fifth Supplement to McCance & Widdowson's The Composition of Foods, 5th ed. Royal Society of Chemistry and Ministry of Agriculture, Fisheries and Food, London: HMSO.

Chan, W., Brown, J., Church, S. M. & Buss, D. H. (1996). Meat Products and Dishes. Sixth Supplement to McCance & Widdowson's The Composition of Foods, 5th ed. Royal Society of Chemistry and Ministry of Agriculture, Fisheries and Food, London: HMSO.

EFSA Panel on Dietetic Products, N., Allergies, Turck, D., Bresson, J.-L., Burlingame, B., Dean, T., Fairweather-Tait, S., Heinonen, M., Hirsch-Ernst, K. I., Mangelsdorf, I., McArdle, H. J., Naska, A., Nowicka, G., Pentieva, K., Sanz, Y., Siani, A., Sjödin, A., Stern, M., Tomé, D., Van Loveren, H., Vinceti, M., Willatts, P., Lamberg-Allardt, C., Przyrembel, H., Tetens, I., Dumas, C., Fabiani, L., Ioannidou, S. & Neuhäuser-Berthold, M. (2017). Dietary reference values for vitamin K. *EFSA Journal,* 15**,** e04780.

Food Standards Agency (2002a). Food Portion Sizes. London: The Stationary Office.

Food Standards Agency 2002b. *McCance and Widdowson's The Composition of Foods, 6th ed,* Cambridge: Royal Society of Chemistry.

Foster E, Hawkins A & Adamson A 2010. *Young Person's Food Atlas: Pre-school. London, Food Standards Agency.*

Foster, E., Hawkins, A. & Adamson, A. 2010. *Young Person's Food Atlas: Primary,* England, Food Standards Agency.

Harrington, K. E., Robson, P. J., Kiely, M., Livingstone, M. B., Lambe, J. & Gibney, M. J. (2001). The North/South Ireland Food Consumption Survey: survey design and methodology. *Public Health Nutrition,* 4**,** 1037-42.

Holland, B., Brown, J. & Buss, D. H. (1993). Fish and Fish Products: Third Supplement to the Fifth Edition of McCance and Widdowson's The Composition of Foods. London: HMSO, Royal Society of Chemistry.

Holland, B., Unwin, I. D. & Buss, D. H. (1992a). Fruit and Nuts: First Supplement to the Fifth Edition of McCance and Widdowson's The Composition of Foods. London: HMSO, Royal Society of Chemistry.

Holland, B., Unwin, I. D., McCance, R. A. & Buss, D. H. (1989). Milk Products and Eggs: Fourth Supplement to McCance and Widdowson's The Composition of Foods. London: HMSO, Royal Society of Chemistry.

Holland, B., Welch, A. & Buss, D. H. (1992b). Vegetable Dishes: Second Supplement to the Fifth Edition of McCance and Widdowson's The Composition of Foods. London: HMSO, Royal Society of Chemistry.

Holland, B., Welch, A., Unwin, I. D., Buss, D. H., Paul, A. A. & Southgate, D. A. T. (1995). McCance and Widdowson's The Composition of Foods, 5th ed. London: HMSO, Royal Society of Chemistry.

Holland, B., Widdowson, E. M., Unwin, I. D. & Buss, D. H. (1991). Vegetables, Herbs and Spices: Fifth Supplement to McCance and Widdowson's The Composition of Foods. London: HMSO, Royal Society of Chemistry.

Holland, B., Widdowson, E. M., Unwin, I. D., McCance, R. A. & Buss, D. H. (1988). Cereal and Cereal Products: Third Supplement to McCance and Widdowson's The Composition of Foods. London: HMSO, Royal Society of Chemistry.

Irish Universities Nutrition Alliance (IUNA) (2012). *The National Pre-school Nutrition Survey (NPNS)* [Online]. Available: http://www.iuna.net/?p=169 [Accessed January 2017].

Lyons, J., Walton, J. & Flynn, A. (2013). Development of an online database of typical food portion sizes in Irish population groups. *Journal of nutritional science,* 2**,** e25-e25.

Nelson M, Atkinson M & Meyer J (1997). A photographic atlas of food portion sizes. England: Food Standards Agency.

Chapter 3

Update of the vitamin K content of the Irish Food Composition Database

Tentative title: A methodology for constructing a food composition database for vitamin K_1 and vitamin K_2

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Introduction

Vitamin K consists of a family of fat soluble compounds which includes vitamin K_1 (phylloquinone) and vitamin K_2 (menaquinones), all of which have a common chemical structure of 2-methyl-1,4 naphthoquinone but differ in the length and degree of saturation of their side chain. Vitamin K_1 has a phytyl side chain and is found in foods of plant origin including green leafy vegetables and certain plant oils (Shearer, 1995, Shearer and Newman, 2008). Menaquinones have repeating unsaturated prenyl side chains of varying lengths, are synthesised by bacteria and are found in foods of animal origin and fermented food products. Menaquinone-4 differs from the other menaquinones in that, it is not synthesized by bacteria; it is produced in mammals from the tissue specific conversion from phylloquinone or menadione (Dialameh *et al.*, 1971, Okano *et al.*, 2008). It has been well established that vitamin K is required for blood coagulation but there is increasing evidence supporting the hypothesis for a role of vitamin K in areas beyond coagulation in bone metabolism and the inhibition of arterial calcification (Booth, 2009, Vermeer, 2012, Halder *et al.*, 2019). A review of the literature (chapter 1) has highlighted that there are few data available on vitamin K intakes in national dietary surveys across Europe or further afield, particularly for menaquinones. This may be partly due to lack of country-specific food composition data for vitamin K and its separate components (phylloquinone and menaquinones) (Shearer and Bolton-Smith, 2000, Elmadfa and Meyer, 2010).

Analytical values for both vitamin K_1 and menaquinone-4 (for a small range of foods) are available in the UK Composition of Foods Integrated Dataset (COFID) and US Department of Agriculture (USDA) National Nutrient Database (Public Health England Composition of Foods Integrated Dataset, 2015, USDA National Nutrient Database for Standard References Release 28, 2015). Other food composition databases include vitamin K values derived using a combination of methods including ‘borrowing’ analysed data from other countries or the literature, HPLC analysis, estimating values via recipe calculation or applying values based on that of similar foods (Technical University of Denmark, 2007, Anses/CIQUAL, 2013, TürKomp Turkish Food Composition Database, 2014, Food Composition Database Italy (BDA), 2015, Dutch Nutrients Database (NEVO), 2016, German Food Code and Nutrient

Database, 2017, Swedish National Food Database, 2017, Finnish National Food Composition Database, 2019). These methods used to assign composition data to foods has been deemed appropriate for estimating nutrient composition when direct chemical analysis is not possible (Rand *et al.*, 1991, Schakel *et al.*, 1997). Composition databases report vitamin K composition in this manner in Denmark and Germany (for vitamin K_1), in France and Turkey (for vitamin K_1 and K_2), in Finland, Sweden and the Netherlands (for total vitamin K) and in Italy (for vitamin K_1, MK-4 and dihydrophylloquinone (formed from the hydrogenation of vitamin K_1 rich oils) (Technical University of Denmark, 2007, Anses/CIQUAL, 2013, TürKomp Turkish Food Composition Database, 2014, Food Composition Database Italy (BDA), 2015, Dutch Nutrients Database (NEVO), 2016, German Food Code and Nutrient Database, 2017, Swedish National Food Database, 2017, Finnish National Food Composition Database, 2019).

It has been highlighted in the literature that when updating food composition data for vitamin K, recipes and composite dishes should be updated at ingredient level (rather than applying average values to similar dishes) as mixed dishes have been acknowledged to be a significant source of vitamin K. Composite dishes, even without vitamin K rich vegetables, may be an important source due to the oils and animal products used in their preparation (Finnan *et al.*, 2017, Harshman *et al.*, 2017).

The Irish food composition database (IFCD) (2012) has been developed over the last 20 years informed by foods consumed on the Irish national dietary surveys carried out by the Irish Universities Nutrition Alliance (IUNA) between 2003 and 2011 (www.iuna.net). For all of the surveys, food and beverage intake data were collected at brand level; and recipes of composite dishes were provided by participants, allowing for the estimation of vitamin K content for each individual food product and recipe. The aim of this study was to update the IFCD (2012) with analytical values for vitamin K_1 and vitamin K_2 (menaquinone-4 (MK-4) and menaquinone-5 to 10 (MK-5-10)), ultimately to allow for the assessment of vitamin K intakes in Irish population groups.

Methods

The IFCD (2012) includes data from four national dietary surveys carried out in the Republic of Ireland; The National Pre-school Nutrition Survey (2010-11), the National Children's Food Survey (2003-04), the National Teens' Food Survey (2005-06) and the National Adult Nutrition Survey (2008-10) (www.iuna.net).

The IFCD (2012) has been updated for each survey to include recipes of composite dishes, nutritional supplements, fortified foods, infant specific products and generic Irish foods that were commonly consumed. Each food and beverage consumed throughout the four surveys was assigned a food code, based on the food descriptor and the nutritional composition of the food. The IFCD (2012) contains 3443 unique food codes.

Vitamin K_1 composition of foods

Analytical sources of vitamin K_1 composition

For vitamin K_1, composition data were sourced from published analytical values from:

- The UK Composition of Foods Integrated Dataset (COFID): This database provided vitamin K_1 composition values for the following food groups; cereal and cereal products, milk and milk products, eggs, fats and oils, meat and meat products, fish and fish products, potatoes, fruit and vegetables (Public Health England Composition of Foods Integrated Dataset, 2015). This composition database contains composition data from a 'provisional' vitamin K_1 composition table by Bolton-Smith *et al.* (2000).
- The USDA National Nutrient Database for Standard Reference Release 28: This database provides vitamin K_1 composition values for approximately 5000 foods from food groups which include; herbs and spices, fruit and vegetables, savouries, fats and oils, meat and meat products, cereal and cereal products (USDA National Nutrient Database for Standard References Release 28, 2015).
- Published papers including those by Booth *et al.* (1993), Bolton-Smith *et al.* (2000), Dismore *et al.* (2003), Presse *et al.* (2015) and Damon *et al.* (2005)

were used to provide composition data where appropriate. Examples of the vitamin K_1 composition of food groups reported in these papers include; herbs and spices, fruit and vegetables, fats and oils, dairy, meat, cereals and beverages.

Assigning vitamin K_1 composition values to the IFCD (2012)

Using the composition sources listed above, the following methods were used to assign vitamin K_1 composition values to all foods in the IFCD (2012);

Published analytical values. Vitamin K_1 composition values provided in the UK COFID or USDA National Nutrient Database and published papers that were an exact match to foods in IFCD (2012) were assigned the equivalent vitamin K_1 composition value.

Similar product. In certain cases, where there was no published composition value for a food, the vitamin K_1 content of a similar product from the UK COFID or USDA National Nutrient Database, or published papers was used. For example, the vitamin K_1 value for corn flakes from the UK COFID was assigned to Frosties as both products have the same ingredients and similar nutrient profile with the exception of sugar content which will not influence vitamin K_1 content.

Recipe calculation. A new recipe file was compiled during each survey for composite dishes consumed. The vitamin K_1 content of each recipe in the IFCD (2012) were calculated from the vitamin K_1 values of the individual ingredients according to the composition databases and published papers utilised. If a recipe contained a specific ingredient that contained vitamin K_1 but no exact vitamin K_1 composition value was available for the ingredient, the value of a similar ingredient was substituted in order to calculate the vitamin K_1 content of the recipe (for example, the vitamin K_1 content of tomato sauce was provided in the USDA National Nutrient Database; this vitamin K_1 value was substituted for all sauces that were tomato based when no other composition value was available). In certain cases where no exact recipe was available, the food code was given the vitamin K_1 value of that of a similar recipe.

Retail product. For retail products where no composition value was available the vitamin K_1 content of the product was calculated on the basis of listed ingredients from manufacturers or product packaging.

Manufacturers' information. The vitamin K_1 composition values of supplements and infant formula were assigned based on nutrition information on packaging or from information provided by the manufacturer.

Foods that did not contain any vitamin K_1 were assigned a composition value of zero. These foods included ham and bacon, sugar based beverages and confectionary sweets such as pastilles, boiled sweets and peppermints (Bolton-Smith *et al.*, 2000).

Other. The vitamin K_1 content of some foods was calculated on the basis of the fat content of a similar product. In a small number of cases where no composition data were available, foods such as seeds and miscellaneous foods were assigned a vitamin K_1 composition value of zero as they were likely to contain negligible amounts of vitamin K_1.

Menaquinone composition of foods

As the menaquinones are synthesised by bacteria (with the exception of MK-4), they are only found in foods of animal origin (meat, dairy, eggs) and fermented food products. Menaquinone composition data were sourced from published analytical values from;

- The UK COFID which provided the MK-4 composition of eggs only (Public Health England Composition of Foods Integrated Dataset, 2015).
- Published papers from Schurgers and Vermeer (2000) and Fu *et al.* (2016). Schurgers and Vermeer (2000) provided the menaquinone composition values for meat, fish, fruit and vegetables, dairy, oils and bread. Fu *et al.* (2016) reported the menaquinone composition values for pork and pork products. Each food code was assigned both an MK-4 composition value and an MK-5-10 composition value.

Assigning vitamin K_2 composition values to the IFCD (2012)

Using the composition sources listed above, the following methods were used to assign MK-4 and MK-5-10 composition values to all foods in the IFCD (2012);

Foods and beverages that were not fermented and were not of animal origin were given a value of zero for all menaquinones.

Recipe calculation. A new recipe file was compiled during each survey for composite dishes consumed. The menaquinone content for each recipe in the IFCD (2012) were calculated from the menaquinone values of the individual ingredients. If a recipe contained a specific ingredient that contained menaquinones but no exact menaquinone composition value was available for the ingredient, the value of a similar ingredient was substituted in order to calculate the menaquinone content of the recipe. (For example, the menaquinone content of plaice was used for all white fish). In certain cases where no exact recipe was available, the food code was given the menaquinone value of that of a similar recipe.

Retail products. The menaquinone content of the food product was calculated based on the ingredients listed on food packaging.

Published analytical values. Menaquinone composition values provided by Schurgers and Vermeer (2000) or Fu *et al.* (2016) were assigned to matching foods in the IFCD (2012) where appropriate.

Similar product. In certain cases, where there was no exact match available for a food, the menaquinone content of a similar food product from the published analytical values was used. (For example, the menaquinone content of chicken meat was used for turkey meat).

Manufacturers' information provided the menaquinone composition values for nutritional supplements and infant formula.

Other. Where no composition data were available for the food product and no other estimation of composition was available a composition value of 0µg was assigned.

Results

Table 1 reports the sources of vitamin K_1 composition data used to update the IFCD (2012) (*n*, %). The UK COFID provided vitamin K_1 composition values for 1058 foods (31%); of which, 348 foods (10%) in the IFCD (2012) were an exact match to foods provided in the UK COFID and 710 foods (21%) were a similar product. The USDA National Nutrient Database provided composition values for 575 foods (17%) in the IFCD (2012); of which, 429 foods (13%) in the IFCD (2012) were an exact match to foods in the USDA National Nutrient Database and 146 foods (4%) were a similar product. Published analytical vitamin K_1 composition data provided vitamin K_1 content values for 179 foods (5%) in the IFCD (2012). Recipes accounted for 1054 food codes (31%) in the IFCD (2012). Of this, the vitamin K_1 content of 870 recipes (25%) were calculated on the basis of their individual ingredients. The vitamin K_1 content of a similar recipe was used for 127 recipes (4%) as details of ingredients were not available. Manufacturers' information provided on the packaging of nutritional supplements and infant formula provided vitamin K_1 composition values for 353 (10%) food codes in the IFCD (2012). One hundred and forty eight foods (4%) that did not contain any vitamin K_1 were assigned a vitamin K_1 composition value of 0µg. For a small number of food codes (*n* 76 (2%)), the vitamin K_1 content was assigned based on the fat content of a similar product or where no composition data were available, foods were assigned a value of zero as they were likely to contain negligible amounts of vitamin $K_{1.}$

Table 2 describes an overview of the vitamin K_1 composition values split by food group in descending order in µg/100g. The 'herbs & spices' food group had a vitamin K_1 composition value ranging from 31 to 3220µg/100g. The vitamin K_1 content of 'vegetable & vegetable dishes' ranged from 0 to 840µg/100g. 'Soups, sauces & miscellaneous foods' and 'oils' had a vitamin K_1 content ranging from 0 to 550µg/100g and 1 to 131µg/100g, respectively. The vitamin K_1 content of 'fruit & fruit juices' and 'meat & meat products' ranged from 0 to 105µg/100g and 0 to 82µg/100g, respectively.

Table 3 reports examples of vitamin K_1 composition values in foods groups that were highest in vitamin K_1 as outlined in table 2. 'Dried herbs' had a vitamin K_1 content ranging from 1168 (mixed herbs, dried) to 3220µg/100g (mint, dried). 'Fresh herbs' had a vitamin K_1 content ranging from 213 (Chives, fresh) to 636µg/100g (Oregano, fresh). The vitamin K_1 content of spices ranged from 31 (cinnamon) to 212µg/100g (allspice). 'Green vegetables and salad vegetables' had a vitamin K_1 content ranging from 1 (shallots, raw) to 840µg/100g (spinach, frozen, boiled). Of this, tomatoes, raw, lettuce, average, raw and broccoli, green, boiled had vitamin K_1 contents of 6, 129 and 135µg/100g, respectively. 'Soups, sauces & miscellaneous foods' had a vitamin K_1 content ranging from 0 (vinegar) to 550µg/100g (mint sauce). Of this, tomato based sauces, cream of vegetable soup and mayonnaise had vitamin K_1 contents of 3, 23 and 43µg/100g, respectively. The vitamin K_1 content of 'vegetable & pulse dishes' ranged from 0 (vegetarian sausages) to 285µg/100g (spinach cream sauce). 'Oils' had a vitamin K_1 content ranging from 1 (peanut oil) to 131µg/100g (soya oil). Of this, sunflower oil, olive oil and blended vegetable oil had vitamin K_1 contents of 6, 58 and 114µg/100g, respectively.

Table 4 describes the sources of menaquinone composition data (menaquinone-4 and menaquinone-5-10) used to update the Irish Food Composition Database (2012) (*n*, %).

Menaquinone- 4

An MK-4 composition value of 0µg was assigned to 1656 foods (48%) that were not fermented and were not of animal origin. The MK-4 composition of 640 recipes (19%) were calculated on the basis of their individual ingredients. When no recipe details were available for a food code, the MK-4 composition value of a similar recipe was assigned (*n* 139 (4%)). Published analytical values as reported by Schurgers and Vermeer (2000) and Fu *et al.* (2016) provided MK-4 composition values for 298 (9%) and 26 (1%) food codes, respectively. For 211 foods, the MK-4 composition value of a similar product as reported in the literature was assigned (6%). Manufacturers' information provided on the packaging of nutritional supplements and infant formula was used to assign MK-4 composition values for 353 (10%) food codes in the IFCD (2012), none of which contained MK-4. A composition value of zero was assigned to 30 (<1%) food codes where there were no composition data available.

Menaquinone-5-10

An MK-5-10 composition value of 0µg was assigned to 1660 foods (48%) that were not fermented and were not of animal origin. The MK-5-10 composition of 640 recipes

(19%) were calculated on the basis of their individual ingredients. When no recipe details were available for a food code, the MK-5-10 composition value of a similar recipe was assigned (*n* 139 (4%)). Published analytical values as reported by Schurgers and Vermeer (2000) and Fu *et al.* (2016) provided MK-5-10 composition values for 298 (9%) and 26 (1%) food codes, respectively. For 211 foods, the MK-5-10 composition value of a similar product was assigned (6%). Manufacturers' information provided on the packaging of nutritional supplements and infant formula was used to assign MK-5-10 composition values for 353 (10%) food codes in the IFCD (2012), none of which contained MK-5-10. A composition value of zero was assigned to 30 (<1%) food codes where there were no composition data available.

Table 5 reports the range of menaquinone (MK-4 & MK-5-10) values in each food group in µg/100g.

Menaquinone-4

The MK-4 content of 'meat & meat products' ranged from 0 to 28µg/100g. Of this, 'sausages' and 'lamb, pork & bacon dishes' had a MK-4 composition ranging from 7 to 28µg/100g and 0 to 11µg/100g, respectively. 'Cheese' and 'eggs & egg dishes' had MK-4 composition values ranging from 0 to 5µg/100g and 2 to 15µg/100g, respectively. The MK-4 content of 'butter, spreading fats & oils' and 'vegetable & vegetable dishes' ranged from 0 to 15 and 0 to 3µg/100g, respectively.

Menaquinone-5-10

The MK-5-10 content of 'meat & meat products' ranged from 0 to 341µg/100g. Of this, 'sausages' and 'lamb, pork & bacon dishes' had a MK-5-10 composition ranging from 0 to 341µg/100g and 0 to 136µg/100g, respectively. 'Cheese' and 'eggs & egg dishes' had MK-5-10 composition values ranging from 24 to 72µg/100g and 0 to 28µg/100g, respectively. The MK-5-10 content of 'vegetable & vegetable dishes' ranged from 0 to 17µg/100g.

Table 1. Sources of vitamin K_1 composition data used to update the Irish Food Composition Database (2012) (*n*, %)

Source of composition data	***n***	**%**
Published analytical values	**1812**	**52.5**
UK COFID nutrient databank	1058	30.7
Of which: Exact match	*348*	*10.1*
Of which: Similar product	*710*	*20.6*
USDA nutrient databank	575	16.7
Of which: Exact match	*429*	*12.5*
Of which: Similar product	*146*	*4.2*
Booth *et al.* (1993)	73	2.1
Bolton-Smith *et al.* (2000)	60	1.7
Dismore *et al.* (2003)	14	0.4
Presse *et al.* (2015)	8	0.2
Damon *et al.* (2005)	8	0.2
Similar product	16	0.5
Recipes	**1054**	**30.6**
Recipe calculated from ingredients list	870	25.2
Similar to calculated recipes	127	3.7
Retail product calculated from ingredients list	58	1.7
Manufacturers information	**353**	**10.2**
Nutritional supplements	340	9.9
Infant formula	13	0.4
Foods that did not contain any vitamin K_1 (assigned value of 0µg)	**148**	**4.3**
Other	**76**	**2.3**
Total	**3443**	**100**

Table 2. Overview of vitamin K_1 composition values (µg/100g) split by food group in descending order

Food group	**µg/100g**	
	Minimum	**Maximum**
Herbs & spices	**31.2**	**3220**
Herbs	*212.7*	*3220*
Spices	*31.2*	*212*
Vegetable & vegetable dishes	**0.0**	**840**
Green vegetables	3.3	840
Vegetable & pulse dishes	0.0	285
Salad vegetables	*0.0*	*207*
Other vegetables	*0.0*	*242*
Peas, beans & lentils	*0.0*	*47.0*
Tinned or jarred vegetables	*0.0*	*41.3*
Soups, sauces & miscellaneous foods	**0.0**	**550**
Oils	**0.7**	**131**
Fruit & fruit juices	**0.0**	**105**
Meat & meat products	**0.0**	**82.4**
Grains, rice, pasta & savouries	0.0	72.1
Biscuits, cakes & pastries	0.0	69.3
Fish & fish dishes	0.0	62.7
Butter & fat spreads	2.6	56.0
Nuts & seeds	0.0	53.9
Eggs & egg dishes	0.0	37.4
Potatoes & potato products	0.8	36.5
Breakfast cereals	0.0	33.0
Creams, ice-creams & chilled desserts	0.0	18.1
Sugars, confectionary, preserves & savoury snacks	0.0	15.5
Milk & yoghurt	0.0	10.0
Bread & rolls	0.3	8.4
Cheese	0.0	4.7
Beverages	0.0	4.3

Table 3. Examples of vitamin K_1 composition values in foods groups highest in vitamin K_1 as outlined in table 2

Food group	µg/100g
Herbs (min-max)	**(213-3220)**
Dried herbs	**(1168-3220)**
Mixed herbs, dried	1168
Basil, dried	1715
Mint, dried	3220
Fresh herbs	**(213-636)**
Chives, fresh	213
Parsley, fresh	548
Oregano, fresh	636
Spices (min-max)	**(31.2-212)**
Cinnamon	31.2
Curry powder	99.8
Allspice	212
Green vegetables and salad vegetables (min-max)	**(0.0-840)**
Shallots, raw	0.8
Tomatoes, raw	6.0
Lettuce, average, raw	129
Broccoli, green, boiled	135
Spring onions, raw	207
Spinach, frozen, boiled	840
Soups, sauces & miscellaneous foods (min-max)	**(0.0-550)**
Vinegar	0.0
Tomato based sauces	2.8
Cream of vegetable soup	23.0
Mayonnaise	43.3
Caesar salad dressing	105
Mint sauce	550
Vegetable & pulse dishes (min-max)	**(0.0-285)**
Vegetarian sausages	0.0
Kidney bean & veg stew	59.5
Caesar salad	108
Spinach cream sauce	285
Oils (min-max)	**(0.7-131)**
Peanut oil	0.7
Sunflower oil	6.3
Olive oil	57.5
Blended vegetable oil	114
Soya oil	131

Table 4. Sources of menaquinone composition data (menaquinone-4 and menaquinone-5-10) used to update the Irish Food Composition Database (2012) (*n*, %)

Source of composition data	**MK-4**		**MK-5-10**	
	n	**%**	***n***	**%**
Foods assigned a composition value of 0µg for MK-4 and MK-5-10	**1656**	**48.1**	**1660**	**48.2**
Recipes	**865**	**25.1**	**865**	**25.1**
Recipes calculated from ingredients list	640	18.6	640	18.6
Similar recipes	139	4.0	139	4.0
Retail product calculated from ingredients list	86	2.5	86	2.5
Published analytical values	***539***	***15.7***	***535***	***15.6***
UK COFID	4	0.1	0	0.0
Schurgers and Vermeer (2000)	298	8.7	298	8.7
Fu et al. (2016)	26	0.8	26	0.8
Similar products	211	6.1	211	6.1
Manufacturers information	**353**	**10.2**	**353**	**10.2**
Nutritional supplements	340	9.9	340	9.9
Infant formula	13	0.4	13	0.4
Other	**30**	**0.9**	**30**	**0.9**
Total	**3443**	**100**	**3443**	**100**

Table 5. Overview of menaquinone (menaquinone-4 and menaquinone-5-10) composition values (µg/100g) split by food group in descending order

Food group	Range of menaquinone values (µg/100g)			
	MK-4		MK-5-10	
	Minimum	**Maximum**	**Minimum**	**Maximum**
Meat & meat products	**0.0**	**27.5**	**0.0**	**341**
Sausages	*6.9*	*27.5*	*0.0*	*341*
Lamb, pork & bacon dishes	*0.0*	*11.0*	*0.0*	*136*
Meat products	*0.0*	*9.0*	*0.0*	*46.0*
Beef & veal dishes	*0.1*	*4.7*	*0.0*	*46.0*
Meat pies & pastries	*0.0*	*6.9*	*0.0*	*84.0*
Burgers	*1.5*	*6.7*	*0.0*	*7.2*
Bacon & ham	*2.1*	*3.4*	*1.6*	*6.7*
Beef & veal	*1.1*	*6.5*	*0.0*	*0.0*
Poultry & game dishes	*0.0*	*7.4*	*0.0*	*2.7*
Lamb	*1.1*	*6.7*	*0.0*	*1.1*
Chicken, turkey & game	*0.0*	*9.0*	*0.0*	*0.0*
Pork	*2.1*	*2.1*	*1.6*	*1.6*
Cheese	**0.4**	**4.7**	**24.4**	**71.6**
Eggs & egg dishes	**2.2**	**15.0**	**0.0**	**28.2**
Butter, spreading fats & oils	**0.0**	**15.0**	**0.0**	**0.2**
Vegetable & vegetable dishes	**0.0**	**3.3**	**0.0**	**16.9**
Creams, ice-creams & chilled desserts	0.0	5.4	0.0	4.2
Grains, rice, pasta & savouries	0.0	0.3	0.0	7.2
Fish & fish dishes	0.0	2.9	0.0	4.7
Potatoes & potato products	0.0	1.4	0.0	7.5
Milk & yoghurt	0.0	1.6	0.0	2.3
Sugars, confectionary& savoury snacks	0.0	1.5	0.0	0.0

Discussion

This aim of this study was to assign both vitamin K_1 and vitamin K_2 composition values to all foods in the IFCD (2012), ultimately to allow for the assessment of intakes in the Irish population. Vitamin K composition values were assigned to all foods in the IFCD (2012) using pre-existing published analytical data, recipe calculation and manufacturers information. Foods highest in vitamin K_1 included 'herbs' and 'vegetable & vegetable dishes'. Foods highest in MK-4 and MK-5-10 included 'meat & meat products', 'cheese' and 'eggs & egg dishes'.

Vitamin K_1

Vitamin K_1 is found in all photosynthetic plants where it functions as an electron carrier in the photosystem I (Reumann, 2013). This form of vitamin K is responsible for over 80% of dietary vitamin K (Schurgers and Vermeer, 2000). Analytical data has shown that vegetables, especially the green vegetables food group are highly concentrated with vitamin K_1 (Bolton-Smith *et al.*, 2000, Schurgers and Vermeer, 2000, Damon *et al.*, 2005, Harshman *et al.*, 2017). Vegetables with a dark leaf colouring (e.g. spinach, frozen, boiled; 840µg/100g) have a much higher vitamin K_1 content than vegetables with a paler colouring (e.g. lettuce, average, raw; 129µg/100g) due to the chlorophyll needed for photosynthesis (Booth, 2012). Although vegetables are considered to be the most important contributor to vitamin K_1 intakes in all population groups, 'herbs' are the most concentrated food with vitamin K_1 (Booth *et al.*, 1996, Harshman *et al.*, 2017, Kingston *et al.*, 2017, Kingston *et al.*, 2018). Presse *et al.* (2015) analysed the vitamin K_1 content of herbs, spices and seasonings and reported that 'herbs', especially dried herbs are the richest food source of vitamin K_1 however, their contribution to intakes may be underestimated due to the difficulty in quantifying herb consumption and gaps in the literature on the vitamin K_1 composition of herbs. Although it has been reported that dried herbs are consumed in such small quantities and likely contribute negligible amounts of vitamin K_1 (Bolton-Smith *et al.*, 2000), the addition of an extra ~3g of dried herbs to the diet may increase vitamin K_1 intakes by up to 100µg (Presse *et al.*, 2015). Even herbs found in retail products such as bread crumbs, salsa and sauces will influence the vitamin K_1 content of the food product (Damon *et al.*, 2005, Ferreira, 2006). In the IFCD (2012), quantities of herbs as low as 0.5g in recipes and mixed dishes were calculated for vitamin K_1 content, many of which had a significant impact on the vitamin K_1 concentration of the recipe; for example, the vitamin K_1 content of potato stuffing in the IFCD (2012) is 36µg/100g of which, 34µg is due to the 2g of thyme contained within the recipe. The inclusion of herbs in the present study may therefore be considered a strength of the study.

The importance of quantifying individual oils with reference to vitamin K_1 has frequently been outlined throughout the literature (Peterson *et al.*, 2002, Finnan *et al.*, 2017). As there are large variations in the vitamin K_1 content of different oils (sunflower oil; 6.3µg/100g vs vegetable oil; 114µg/100g), this will have a substantial influence on the vitamin K_1 content of the recipe or food product in which it was used and therefore it is important to consider each oil individually and not apply average values to oils used within composite meals and mixed dishes (for example; a tablespoon of sunflower oil equates to 0.95µg of vitamin K_1 versus a tablespoon of blended vegetable oil that equates to 17.2µg of vitamin K_1). Plant oils, salad dressings and cooking sauces made with vitamin K_1 rich oils contain a high vitamin K_1 content (for example, caesar salad dressing; 105µg/100g) all of which influence the vitamin K_1 content of the food product or dish. Even fast foods and take away foods may have high amounts of vitamin K_1 partly due to the plant oils in which they are cooked (Dumont *et al.*, 2003, Weizmann *et al.*, 2004, Elder *et al.*, 2006).

Mixed dishes have been reported as important sources of vitamin K (Finnan *et al.*, 2017, Harshman *et al.*, 2017). 'Vegetable & vegetable dishes' had a large vitamin K_1 composition range (0-840µg/100g) in the IFCD (2012) due to the different vegetables and oils used in their preparation (for example, spinach and potato curry; 144µg/100g versus chicken curry; 6.9µg/100g). Even mixed dishes that do not contain vitamin K_1 rich vegetables can contain moderate amounts of the vitamin from the plant oils or the vitamin K_1 containing oils in dressings or condiments consumed with the dish (Finnan *et al.*, 2017). For example, in the IFCD (2012), a homemade oil and lemon dressing (made with blended vegetable oil) has a vitamin K_1 content of 83µg/100g. Although meat and poultry are not rich sources of vitamin K_1 (Booth *et al.*, 1995, Elder *et al.*, 2006), the ‘meat & meat products’ food group had a moderate vitamin K_1 composition range of 0-82µg/100g. Of this food group, ‘lamb dumplings’ had the highest concentration of vitamin K_1 due to the cabbage and vegetable oil included in the composite dish. By contrast, a chicken casserole in the IFCD (2012) had a vitamin K_1 content of <1µg/100g as it contained vegetables which have negligible amounts of vitamin K_1 and no plant oil. This demonstrates the importance of not applying average values to recipes and assessing each recipe and composite dish individually.

Vitamin K_2

In Ireland and Europe, there are no food composition datasets that are complete for the menaquinones. MK-4 is alkylated from menadione (vitamin K_3) in mammals, which is present in some animal feeds or is the product of tissue-specific conversion from dietary phylloquinone using menadione as an intermediate during the conversion (Dialameh *et al.*, 1971, Thijssen *et al.*, 2006, EFSA Panel on Additives and Products or Substances used in Animal Feed, 2014). It has been reported that up to 25% of dietary phylloquinone may be converted to MK-4 (Shearer *et al.*, 2012). The addition of menadione to animal feeds has been deemed safe and is a common practice in many countries including Ireland (personal contact with manufacturers) and the countries in which composition data were borrowed for this study (National Research Council, 1987, EFSA Panel on Additives and Products or Substances used in Animal Feed, 2014). Foods highest in MK-4 include meats, eggs and dairy and it has been found in substantial concentrations in some mixed dishes and animal food products (Schurgers and Vermeer, 2000, Elder *et al.*, 2006, Fu *et al.*, 2016, Finnan *et al.*, 2017, Fu *et al.*, 2017). In the IFCD (2012), ‘meat & meat products’ had a MK-4 content ranging from 0-28µg/100g. Of this, the highest MK-4 concentration is in sausages. Fu *et al.* (2016) analysed the MK-4 content of processed and fresh cut pork products in the US and reported that the fat content of processed pork products was strongly associated with total vitamin K content. Pork sausages had a high fat content and thus a high MK-4 concentration (27.5µg/100g). In the IFCD (2012), there are large ranges of MK-4 content between different meat products and meat containing recipes depending on the type of meat present. For example, the MK-4 composition of a chicken curry is 3.6µg/100g versus 0.3µg/100g for a beef curry, both of which have similar non-meat ingredients. Even different forms of breakfast options have varying MK-4 concentration depending on the animal products chosen; the MK-4 composition of a bacon and egg breakfast sandwich was 1.8µg/100g versus 4.0µg/100g in a sandwich containing sausage, egg and cheese (Ferreira, 2006). These findings are a further indication of the need to assess all foods individually not only for vitamin K_1 but also for menaquinones to prevent the underestimation of vitamin K content.

The longer chained menaquinones (MK-5-10) are exclusively synthesized by bacteria and a review of the literature has highlighted a lack of composition data for these forms of vitamin K_2 (Walther and Chollet, 2017). Fermentation conditions and the types of bacterial strains used in the production process influence the concentrations and types of menaquinones present in the fermented food product (Walther *et al.*, 2013). In the IFCD (2012), the MK-5-10 content of foods is highest in the following groups; 'meat & meat products', 'cheese', and 'eggs & egg dishes'. Of the limited composition data available, high concentrations of the long chained menaquinones have been reported in cheese (24-72µg/100g) (Schurgers and Vermeer, 2000). Recent findings suggest that cheese may be the most important source of long chain menaquinones in the Western diet with different menaquinone concentrations in cheese depending on fat content, fermentation conditions, bacterial starter culture and geographical location (Vermeer *et al.*, 2018). By contrast, a recent study in the US was the first to report a high menaquinone concentration in pork products (for example, sausages; MK-10 300µg/100g). These differences may be attributed to variations in animal feeds between farms (Vermeer *et al.*, 2018). In the IFCD (2012), of the 'meat & meat products' food group, 'sausages' contained the highest MK-5-10 concentration (341µg/100g) followed by the 'cheese' food group (72µg/100g). Meat products and dishes containing sausages, cheese or both had high MK-5-10 concentration in the IFCD (2012) (for example, sausage and bacon risotto; 75µg/100g, cheese omelette; 25µg/100g). There were large differences in the concentration of MK-5-10 within individual recipes and mixed dishes depending on the type of meat and dairy ingredients, highlighting the importance of assessing each food as a separate entity.

Strengths and limitations

The strengths of the present study include the high quality food consumption data available to conduct our analysis, which was collected at brand level in addition to collection of recipes of composite dishes at ingredient level. This allowed the vitamin K content of each food code to be assessed individually. Packaging was collected from participants of the national dietary surveys allowing an assessment of ingredients in retail products including nutritional supplements and infant formula. The subjective method of assigning vitamin K composition values to all food codes may be a limitation of this study however, values were assigned using the most suitable data reflective of foods on the Irish market and the method used in this study has been deemed appropriate for estimating nutrient composition when direct chemical analysis is not possible (Rand *et al.*, 1991, Schakel *et al.*, 1997). Additionally stringent quality control measures were applied to the construction of the database with each value assigned being checked and reviewed to ensure the best estimate of vitamin K content for the products on the Irish market.

Conclusion

This is the first study to assign vitamin K_1 and vitamin K_2 composition values to all foods and beverages in the IFCD (2012), ultimately to allow for the estimation of vitamin K intakes and sources in the Irish population. Published analytical values for vitamin K included in the UK COFID, USDA National Nutrient Database and published papers were used to assign vitamin K composition values to all foods and beverages. This composition database will add to the limited vitamin K composition data currently available in Ireland and will aid industry and public health researchers in the assessment of intakes at population level. Future researchers should consider the need for analytical values for the vitamin K content of foods in the Irish market place.

References

Anses/CIQUAL. 2013. *French food composition table version 2013* [Online]. Available: https://pro.anses.fr/TableCIQUAL/ [Accessed 2017].

Bolton-Smith, C., Price, R. J., Fenton, S. T., Harrington, D. J. & Shearer, M. J. (2000). Compilation of a provisional UK database for the phylloquinone (vitamin K1) content of foods. *British Journal of Nutrition,* 83**,** 389-99.

Booth, S. L. (2009). Roles for vitamin K beyond coagulation. *The Annual Review of Nutrition,* 29**,** 89-110.

Booth, S. L. (2012). Vitamin K: food composition and dietary intakes. *Food & Nutrition Research,* 56.

Booth, S. L., Pennington, J. A. & Sadowski, J. A. (1996). Food sources and dietary intakes of vitamin K-1 (phylloquinone) in the American diet: data from the FDA Total Diet Study. *Journal of the American Dietetic Association,* 96**,** 149-54.

Booth, S. L., Sadowski, J. A. & Pennington, J. A. T. (1995). Phylloquinone (Vitamin K1) Content of Foods in the U.S. Food and Drug Administration's Total Diet Study. *Journal of Agricultural and Food Chemistry,* 43**,** 1574-1579.

Booth, S. L., Sadowski, J. A., Weihrauch, J. L. & Ferland, G. (1993). Vitamin K1 (Phylloquinone) Content of Foods: A Provisional Table. *Journal of Food Composition and Analysis,* 6**,** 109-120.

Damon, M., Zhang, N. Z., Haytowitz, D. B. & Booth, S. L. (2005). Phylloquinone (vitamin K1) content of vegetables. *Journal of Food Composition and Analysis,* 18**,** 751-758.

Dialameh, G. H., Taggart, W. V., Matschiner, J. T. & Olson, R. E. (1971). Isolation and characterization of menaquinone-4 as a product of menadione metabolism in chicks and rats. *International Journal for Vitamin and Nutrition Research,* 41**,** 391-400.

Dismore, M. L., Haytowitz, D. B., Gebhardt, S. E., Peterson, J. W. & Booth, S. L. (2003). Vitamin K content of nuts and fruits in the US diet. *Journal of the American Dietetic Association,* 103**,** 1650-2.

Dumont, J. F., Peterson, J., Haytowitz, D. & Booth, S. L. (2003). Phylloquinone and dihydrophylloquinone contents of mixed dishes, processed meats, soups and cheeses. *Journal of Food Composition and Analysis,* 16**,** 595-603.

Dutch Nutrients Database (NEVO). 2016. Available: https://www.rivm.nl/en/dutch-food-composition-database [Accessed 2017].

EFSA Panel on Additives and Products or Substances used in Animal Feed (2014). Scientific Opinion on the safety and efficacy of vitamin K3 (menadione sodium bisulphite and menadione nicotinamide bisulphite) as a feed additive for all animal species. *EFSA Journal,* 12**,** 3532.

Elder, S. J., Haytowitz, D. B., Howe, J., Peterson, J. W. & Booth, S. L. (2006). Vitamin k contents of meat, dairy, and fast food in the u.s. Diet. *Journal of Agricultural and Food Chemistry,* 54**,** 463-7.

Elmadfa, I. & Meyer, A. L. (2010). Importance of food composition data to nutrition and public health. *European Journal of Clinical Nutrition,* 64 Suppl 3**,** S4-7.

Ferreira, D. W. (2006). Vitamin K Contents of Grains, Cereals, Fast-Food Breakfasts, and Baked Goods. *Journal of Food Science,* 71**,** S66-S70.

Finnan, E. G., Harshman, S. G., Haytowitz, D. B. & Booth, S. L. (2017). Mixed dishes are an unexpected source of dietary vitamin K. *Journal of Food Composition and Analysis,* 64**,** 127-131.

Finnish National Food Composition Database. 2019. *National Institute for Health and Welfare.* [Online]. Available: https://fineli.fi/fineli/en/index [Accessed 2017].

Food Composition Database Italy (BDA). 2015. *European Institute of Oncology 2015* [Online]. Available: http://www.bda-ieo.it/ [Accessed 2017].

Fu, X., Harshman, S. G., Shen, X., Haytowitz, D. B., Karl, J. P., Wolfe, B. E. & Booth, S. L. (2017). Multiple Vitamin K Forms Exist in Dairy Foods. *Current Developments in Nutrition,* 1**,** e000638-e000638.

Fu, X., Shen, X., Finnan, E. G., Haytowitz, D. B. & Booth, S. L. (2016). Measurement of Multiple Vitamin K Forms in Processed and Fresh-Cut Pork Products in the U.S. Food Supply. *Journal of Agricultural and Food Chemistry,* 64**,** 4531-5.

German Food Code and Nutrient Database. 2017. *Bundeslebensmittelschlüssel version 3.02* [Online]. Max Rubner Institut. Available: https://www.blsdb.de/ [Accessed 2017].

Halder, M., Petsophonsakul, P., Akbulut, A. C., Pavlic, A., Bohan, F., Anderson, E., Maresz, K., Kramann, R. & Schurgers, L. (2019). Vitamin K: Double Bonds beyond Coagulation Insights into Differences between Vitamin K1 and K2 in Health and Disease. *International Journal of Molecular Sciences,* 20**,** 896.

Harshman, S. G., Finnan, E. G., Barger, K. J., Bailey, R. L., Haytowitz, D. B., Gilhooly, C. H. & Booth, S. L. (2017). Vegetables and Mixed Dishes Are Top Contributors to Phylloquinone Intake in US Adults: Data from the 2011-2012 NHANES. *Journal of Nutrition,* 147**,** 1308-1313.

Kingston, C., Kehoe, L., McNulty, B. A., Nugent, A. P., Cashman, K. D., Walton, J. & Flynn, A. (2018). Intakes and sources of vitamin K1 in Irish teenagers aged 13–17 years. *Proceedings of the Nutrition Society,* 77**,** E77.

Kingston, C., Kehoe, L., Walton, J., McNulty, B. A., Nugent, A. P., Cashman, K. D. & Flynn, A. (2017). Intakes and sources of Vitamin K1 in Irish pre-school children aged 1–4 years. *Proceedings of the Nutrition Society,* 76**,** E52.

National Research Council 1987. *Vitamin Tolerance of Animals,* Washington, DC, The National Academies Press.

Okano, T., Shimomura, Y., Yamane, M., Suhara, Y., Kamao, M., Sugiura, M. & Nakagawa, K. (2008). Conversion of phylloquinone (Vitamin K1) into menaquinone-4 (Vitamin K2) in mice: two possible routes for menaquinone-4 accumulation in cerebra of mice. *Journal of Biological Chemistry,* 283**,** 11270-9.

Peterson, J. W., Muzzey, K. L., Haytowitz, D., Exler, J., Lemar, L. & Booth, S. L. (2002). Phylloquinone (vitamin K1) and dihydrophylloquinone content of fats and oils. *Journal of the American Oil Chemists' Society,* 79**,** 641-646.

Presse, N., Potvin, S., Bertrand, B., Calvo, M. S. & Ferland, G. (2015). Phylloquinone content of herbs, spices and seasonings. *Journal of Food Composition and Analysis,* 41**,** 15-20.

Public Health England Composition of Foods Integrated Dataset. 2015. *McCance and Widdowson's The Composition of Foods Integrated Dataset 2015* [Online]. Available: https://www.gov.uk/government/publications/composition-of-foods-integrated-dataset-cofid.

Rand, W., A T Pennington, J., P Murphy, S. & Klensin, J. 1991. *Compiling data for food composition data bases,* Tokyo, United Nations University Press.

Reumann, S. (2013). Biosynthesis of vitamin K1 (phylloquinone) by plant peroxisomes and its integration into signaling molecule synthesis pathways. *Sub-Cellular Biochemistry,* 69**,** 213-29.

Schakel, S., Buzzard, I. M. & E. Gebhardt, S. 1997. *Procedures for Estimating Nutrient Values for Food Composition Databases*.

Schurgers, L. J. & Vermeer, C. (2000). Determination of phylloquinone and menaquinones in food. Effect of food matrix on circulating vitamin K concentrations. *Haemostasis,* 30**,** 298-307.

Shearer, M. J. (1995). Vitamin K. *The Lancet,* 345**,** 229-234.

Shearer, M. J. & Bolton-Smith, C. (2000). The UK food data-base for vitamin K and why we need it. *Food Chemistry,* 68**,** 213-218.

Shearer, M. J., Fu, X. & Booth, S. L. (2012). Vitamin K nutrition, metabolism, and requirements: current concepts and future research. *Advances in Nutrition,* 3**,** 182-95.

Shearer, M. J. & Newman, P. (2008). Metabolism and cell biology of vitamin K. *Thrombosis and Haemostasis,* 100**,** 530-47.

Swedish National Food Database. 2017. *National Food Administration Sweden* [Online]. Available: https://www.livsmedelsverket.se/om-oss [Accessed 2017].

Technical University of Denmark. 2007. *The official Danish Food Composition Database* [Online]. Available: http://www.foodcomp.dk/v7/fcdb_default.asp [Accessed January 2016].

Thijssen, H. H., Vervoort, L. M., Schurgers, L. J. & Shearer, M. J. (2006). Menadione is a metabolite of oral vitamin K. *British Journal of Nutrition,* 95.

TürKomp Turkish Food Composition Database. 2014. Available: http://turkomp.gov.tr/database?type=foods [Accessed 2017].

USDA National Nutrient Database for Standard References Release 28. 2015. Washington (DC): USDA Agricultural Research Service. Available: http://www.ars.usda.gov/nutrientdata [Accessed January 2016].

Vermeer, C. (2012). Vitamin K: the effect on health beyond coagulation – an overview. *Food & Nutrition Research,* 56**,** 10.3402/fnr.v56i0.5329.

Vermeer, C., Raes, J., van 't Hoofd, C., Knapen, M. H. J. & Xanthoulea, S. (2018). Menaquinone Content of Cheese. *Nutrients,* 10.

Walther, B. & Chollet, M. (2017). Menaquinones, Bacteria, and Foods: Vitamin K2 in the Diet. *In:* GORDELADZE, P. (ed.) *Vitamin K2 vital for health and wellbeing.* InTech.

Walther, B., Karl, J. P., Booth, S. L. & Boyaval, P. (2013). Menaquinones, bacteria, and the food supply: the relevance of dairy and fermented food products to vitamin K requirements. *Advances in Nutrition,* 4**,** 463-73.

Weizmann, N., Peterson, J. W., Haytowitz, D., Pehrsson, P. R., Jesus, V. P. d. & Booth, S. L. (2004). Vitamin K content of fast foods and snack foods in the US diet. *Journal of Food Composition and Analysis,* 17**,** 379-384.

Chapter 4

Intakes and sources of vitamin K_1 (phylloquinone) in Irish children aged 1 to 17 years

Tentative title: Intakes of vitamin K_1 in Irish children aged 1-17 years

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Introduction

Vitamin K is the name given to a family of fat-soluble compounds with a common chemical structure of 3- substituted 2-methyl-1,4 napthoquinone. The traditional role of vitamin K is in blood coagulation however, evidence suggests a role for vitamin K beyond coagulation in roles such as bone turnover and the inhibition of arterial calcification in adults (Booth, 2009, Vermeer, 2012, Halder *et al.*, 2019). In children, it has been shown that a better vitamin K status is associated with a more pronounced increase in bone mineral content (O'Connor *et al.*, 2007, Van Summeren *et al.*, 2008). In addition, it has been reported that a better vitamin K status was associated with decreased bone turnover (Kalkwarf et al., 2004).

Vitamin K_1 (phylloquinone) is the predominant form of vitamin K in the diet and is found in foods such as green leafy vegetables and certain plant oils (Bolton-Smith *et al.*, 2000). As there is no single biomarker to assess vitamin K status, an Estimated Average Requirement (EAR) cannot be established. In its absence, the European Food Safety Authority (EFSA) has set an Adequate Intake (AI) of 1µg phylloquinone per kg bodyweight per day for both adults and children based on its function in blood coagulation (EFSA Panel on Dietetic Products *et al.*, 2017).

There are few data available regarding vitamin K_1 intakes in children and teenagers. A review of vitamin K intakes from national dietary surveys in Europe (Chapter 1) found that only two countries in Europe (Austria and Greece (assumed to be vitamin K_1)) have reported intakes of vitamin K_1 in children and teenagers (Manios *et al.*, 2008, Elmadfa *et al.*, 2012). Intakes have also been reported in the UK (Prynne *et al.*, 2005) and by the National Health and Nutrition Examination Survey in America (US Department of Agriculture, 2018). For children aged 3-12 years, mean intakes ranged from 24-75µg/d and for teenagers aged 13-17 years 61-79 µg/d. In Ireland, the intake of vitamin K_1 in adults aged 18-90 years has previously been published, (Hayes *et al.*, 2016) however, there are no data published on intakes of vitamin K_1 in other population groups (with the exception of preliminary estimates for children aged 5-12y using limited food composition data) (Hannon *et al.*, 2007). Detailed dietary intake data are available from three national food consumption surveys in Ireland: The National Pre-School Nutrition Survey of 1-4 year olds (NPNS) (2010-11), the National Children's Food Survey of 5-12 year olds (NCFS) (2003-04) and the National Teens'

Food Survey of 13-17 year olds (NTFS) (2005-06). This chapter aims to use data from these surveys to estimate the intakes, sources and adequacy of vitamin K_1 in Irish children and teenagers.

Methodology

The analysis for this chapter is based on data from three nationally representative dietary surveys of the Irish population; the National Pre-school Nutrition Survey (NPNS) of 1-4 year olds (2010-11), the National Children's Food Survey (NCFS) of 5-12 year olds (2003-04) and the National Teens' Food Survey (NTFS) of 13-17 year olds (2005-06) (www.iuna.net). The methodology for sampling, participant recruitment, data collection and food quantification for these surveys is described in chapter 2. The methods used when updating the vitamin K_1 content of foods in the IFCD (2012) are outlined in detail in chapter 3. Methods specific to this chapter are outlined below.

Food intake data collection and quantification

Food and beverage intake data were estimated for 500 pre-school children aged 1-4 years in the NPNS using a 4-day weighed food record. The fieldworker visited each participant 3 times over the recording period. For the NCFS, 594 children aged 5-12 years completed a 7-day weighed food record with a total of four visits from the fieldworker over the recording period. Similarly, 441 teenagers aged 13-17 years completed the NTFS using a 7-day semi-weighed food record with four visits from the fieldworker over the recording period.

For each survey, detailed information relating to the amount, type, cooking method, leftovers, packaging and brand of all foods and beverages (including nutritional supplements) consumed over the recording period was collected. Details of recipes of composite dishes were also recorded.

All food and beverage items consumed across the four surveys were quantified via one of the following methods; weighed (using the digital food scales provided to each participant), age appropriate photographic food atlases (Nelson. *et al.*, 1997, Foster. *et al.*, 2010), standard portion weights (Food Standards Agency, 2002, Lyons *et al.*, 2013) and household measures (such as teaspoon, tablespoon, pint etc).

Data entry

Each food and beverage consumed was assigned a unique food code depending on its nutritional profile. Dietary data were then entered into the data entry system WISP©

(Tinuviel Software, Anglesey, UK). A separate database (food file) was created for each survey with one line of data for each food and drink item consumed.

Quality control

A number of quality procedures were put in place in an attempt to minimise error and ensure consistency throughout the collection and data entry of food intake. Each fieldworker was primarily responsible for the collection, quantification, coding and data entry of their own participants' food diaries in an attempt to maintain consistency.

Vitamin K_1 composition data

As described in Chapter 3, each food code was assigned a vitamin K_1 composition value using data from the UK Composition Of Foods Integrated Dataset (COFID) (Public Health England Composition of Foods Integrated Dataset, 2015), United States Department of Agriculture (USDA) National Nutrient Database (USDA National Nutrient Database for Standard References Release 28, 2015), published papers (Booth *et al.*, 1993, Bolton-Smith *et al.*, 2000, Dismore *et al.*, 2003, Damon *et al.*, 2005, Presse *et al.*, 2015), manufacturers' information and recipe calculation.

Anthropometric measurements

For each survey, the body weight of the child was measured in duplicate (to the nearest 0.1kg) in the participant's own homes. More details are available in Chapter 2.

Statistical analysis

Statistical analyses were carried out using SPSS© for Windows™ Version 22.0. The Mean Daily Intake (MDI) of vitamin K_1 was estimated and differences in intakes between gender and age groups were assessed using independent sample T-tests regardless of normality (due to the large sample size). As sample size increases so does the robustness of t-tests to identify deviations from normality, thus parametric tests are recommended for large samples (Fagerland, 2012). To minimise type 1 errors (as a result of multiple testing), the Bonferoni adjustment was used by dividing the alpha level (0.05) by the number of comparisons. Therefore, intakes were considered to be significantly different from each other if $P<0.01$. All data were not normally distributed. The non-parametric Kruskal- Wallis test was used to determine significant differences between independent groups. Where significant differences were identified by the Kruskal- Wallis test, the Mann Whitney U test was used to identify where these differences occurred.

To estimate the key dietary sources of vitamin K_1, all food and drinks consumed were allocated to one of nineteen food groups (Appendix I) and then further subdivided into 68 food groups (NCFS & NTFS) or 77 food groups (NPNS) (Appendix II). The percent contribution of each food group to the MDI of vitamin K_1 was calculated by the mean proportion method (Krebs-Smith *et al.*, 1989) and the key contributors to intakes were determined in order of importance for each age group. This method provides information about the sources that are contributing to the nutrient intake 'per person' and is the preferred method when determining important food sources of a nutrient for individuals in the population group as opposed to investigating the sources of a nutrient within the food supply.

Results

Mean daily intake of vitamin K_1 (µg/d & µg/kg/d)

Table 1 presents the mean daily intake of vitamin K_1 in Irish children aged 1 to 17 years split by gender and age group for each survey group in µg/d. The MDI of vitamin K_1 in pre-school children aged 1-4 years was 32.3µg/d and 39.9µg/d for school children aged 5-12 years. The MDI of vitamin K_1 in teenagers aged 13-17 years was 55.2µg/d. The MDI of vitamin K_1 was significantly (P=0.000) different between all survey groups and there were no differences in mean intakes between boys and girls in any survey group.

Table 2 presents the mean daily intake of vitamin K_1 in Irish children aged 1 to 17 years split by gender and age group for each survey group in µg/kg bodyweight/d. Expressed as a function of body weight (µg/kg bodyweight/d), the MDI of vitamin K_1 in 1-4 year olds, 5-12 year olds and 13-17 year olds was 2.2, 1.3 and 0.9µg/kg/d, respectively.

The MDI (µg/kg/d) of vitamin K_1 in pre-school children aged 1-4 years and children aged 5-12 years were above the AI of 1µg/kg/d. Intakes in teenagers aged 13-17 (0.9µg/kg/d) years were below the AI for each gender/age group examined with the exception of younger teenage boys. Expressed as a function of body weight, the MDI of vitamin K_1 was significantly (P=0.000) different between all survey groups and there were no differences in mean intakes between boys and girls in any survey group.

Key sources of vitamin K_1

1 year olds

Table 3 presents the key food groups that contributed to the mean daily intake of vitamin K_1 in Irish pre-school children aged 1 to 4 years. For 1 year olds, 'vegetable & vegetable dishes' was the key source of vitamin K_1 (26%). Of this, 'green vegetables' was the highest contributor at 14%. 'Milks' contributed 23% of the MDI of vitamin K_1, of which 15% came from 'fortified infant & young child formula'. 'Fruit & fruit juices' contributed 17% of the MDI of vitamin K_1. 'Meat & meat products' contributed 10% of the MDI of vitamin K_1. 'Potatoes & potato products', butter, spreading fats & oils' and 'biscuits, cakes & pastries' each contributed 4% of vitamin K_1 intake for 1 year olds.

2-4 year olds

'Vegetable & vegetable dishes' was the key source of vitamin K_1 (23%-31%) in pre-school children aged 2-4 year olds. Of this, 'green vegetables' accounted for between 12-19% of vitamin K_1 intake. 'Fruit & fruit juices' contributed 16-19% of the MDI of vitamin K_1. At age 2 years, 'milks' accounted for 13% of vitamin K_1 intake, of which, 8% came from 'fortified infant & young child formula'. At age 3 and 4 years, 'milks' contributed 7 and 5% of the MDI of vitamin K_1, respectively. 'Meat & meat products' (11-12%) and 'butter, spreading fats & oils' (7-8%) were also important contributors to the MDI of vitamin K_1 in this age group.

5-12 year olds by gender and age group

Table 4 and Table 5 report the contribution of food groups to the mean daily intake of vitamin K_1 in Irish children aged 5 to 12 years by gender and age group. 'Vegetable & vegetable dishes' was the key source of vitamin K_1 in Irish children aged 5-12 years (29%). Of this, 'green vegetables' contributed 16%. 'Potatoes & potato products' contributed 15% of the MDI of vitamin K_1, of which, 12% came from 'chipped, fried & roasted potatoes'. 'Meat & meat products' 'butter, spreading fats & oils' and 'fruit & fruit juices' contributed 11, 9 and 7% of the MDI of vitamin K_1, respectively.

13 to 17 year olds by gender and age group

Table 6 and Table 7 present the key food groups that contributed to the mean daily intake of vitamin K_1 in Irish teenagers aged 13 to 17 years by gender and age group. 'Vegetable & vegetable dishes' was the key source of vitamin K_1 in 13-17 year olds (32%). Of this, 'green vegetables' contributed 15%. 'Potatoes & potato products' contributed 17% of the MDI of vitamin K_1, of which, 14% came from 'chipped, fried & roasted potatoes'. 'Meat & meat products' contributed 13% of the MDI of vitamin K_1, of which, 5% came from 'meat dishes'. 'Butter, spreading fats & oils' and 'soups, sauces & miscellaneous foods' contributed 8 and 5% of the MDI of vitamin K_1, respectively.

Table 1. The mean daily intake of vitamin K_1 (µg/d) in children aged 1-17 years by gender and age group

Age (years)	µg/d												P- value
	Total				Boys				Girls				
	Mean	SD	Median	IQR	Mean	SD	Median	IQR	Mean	SD	Median	IQR	
1-4 y (*n* 500)	**32.3[a]**	**22.7**	**26.9**	**18.4-38.9**	**32.3**	**23.6**	**26.8**	**18.1-39.1**	**32.3**	**21.7**	**27.1**	**18.7-38.4**	**0.711**
1 y (*n* 126)	34.3	25.5	28.9	17.2-43.2	38.5	32.8	30.1	16.2-49.0	30.1	14.2	28.0	18.9-37.6	
2 y (*n* 124)	31.2	21.4	25.2	18.4-37.3	32.4	25.0	25.9	17.9-38.4	29.9	16.8	23.4	18.6-36.1	
3 y (*n* 126)	30.0	19.0	25.8	18.1-36.1	27.8	18.2	23.3	16.0-35.3	32.0	19.7	28.1	19.2-41.2	
4 y (*n* 124)	33.7	24.2	27.2	20.0-40.3	30.3	12.6	27.3	21.4-39.1	37.2	31.8	26.4	17.7-45.3	
5-12 y (*n* 594)	**39.9[b]**	**23.8**	**33.2**	**24.3-49.2**	**39.8**	**24.0**	**32.4**	**24.9-49.5**	**39.9**	**23.6**	**34.0**	**23.7-48.5**	**0.957**
5-8 y (*n* 296)	37.6	22.5	30.7	22.3-46.0	36.7	21.1	30.6	23.7-45.7	38.6	23.9	31.3	21.0-47.0	
9-12 y (*n* 298)	42.1	24.8	35.2	26.1-51.4	42.8	26.2	35.4	27.0-52.5	41.3	23.3	35.0	26.0-49.2	
13-17 y (*n* 441)	**55.2[c]**	**31.3**	**49.7**	**33.5-69.2**	**59.8**	**35.2**	**53.1**	**35.7-77.1**	**50.5**	**25.8**	**45.5**	**30.7-62.6**	**0.004**
13-14 y (*n* 188)	53.9	28.1	48.2	32.9-69.6	58.7	28.8	54.4	36.9-79.6	49.1	26.8	44.6	29.6-62.5	
15-17 y (*n* 253)	56.1	33.4	50.2	35.1-69.2	60.6	39.4	51.3	35.4-75.5	51.5	25.1	47.3	32.8-63.0	

Differences between gender were assessed using Mann-Whitney U tests with significant differences ($P<0.01$) denoted by *

Differences between age groups were assed using a Kruscal Wallis test ($P=0.000$) with differences denoted by different superscript lower case letters

Vitamin K_1 intakes in 1-4y olds were different than 5-12 year olds ($P=0.000$) and 13-17 year olds ($P= 0.000$); Vitamin K_1 intakes in 5-12 year olds were different than 13-17 year olds ($P =0.000$)

Table 2. The mean daily intake of vitamin K_1 (µg/kg/d) in children aged 1-17 years by gender and age group

Age (years)	µg/kg/d												P- value
	Total				**Boys**				**Girls**				
	Mean	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**	
1-4 y (*n* 497)	**2.2[a]**	**1.7**	**1.7**	**1.2-2.7**	**2.2**	**2.0**	**1.6**	**1.1-2.5**	**2.2**	**1.4**	**1.8**	**1.3-2.8**	**0.126**
1 y (*n* 126)	3.0	2.3	2.4	1.5-3.8	3.3	2.9	2.4	1.3-4.0	2.6	1.3	2.3	1.6-3.6	
2 y (*n* 122)	2.3	1.6	1.7	1.3-2.8	2.3	1.8	1.7	1.3-3.0	2.2	1.3	1.7	1.3-2.7	
3 y (*n* 126)	1.8	1.2	1.5	1.0-2.2	1.6	1.3	1.3	0.9-2.0	2.0	1.1	1.6	1.2-2.5	
4 y (*n* 123)	1.8	1.4	1.5	1.1-2.2	1.7	0.7	1.5	1.1-2.1	2.0	1.8	1.4	1.1-2.6	
5-12 y (*n* 594)	**1.3[b]**	**0.8**	**1.1**	**0.8-1.6**	**1.3**	**0.8**	**1.1**	**0.8-1.5**	**1.3**	**0.8**	**1.0**	**0.8-1.6**	**0.553**
5-8 y (*n* 296)	1.5	0.9	1.2	0.9-1.9	1.5	0.9	1.3	0.9-1.7	1.5	0.9	1.2	0.9-1.9	
9-12 y (*n* 298)	1.1	0.7	0.9	0.7-1.4	1.1	0.8	0.9	0.7-1.4	1.0	0.6	0.9	0.6-1.3	
13-17 y (*n* 332)	**0.9[c]**	**0.5**	**0.8**	**0.6-1.1**	**1.0**	**0.6**	**0.8**	**0.6-1.2**	**0.9**	**0.5**	**0.8**	**0.6-1.1**	**0.630**
13-14 y (*n* 146)	1.0	0.6	0.8	0.6-1.3	1.0	0.6	0.8	0.6-1.4	0.9	0.6	0.8	0.6-1.1	
15-17 y (*n* 186)	0.9	0.5	0.8	0.5-1.1	0.9	0.5	0.7	0.5-1.0	0.9	0.5	0.8	0.5-1.1	

Differences between gender were assessed using Mann-Whitney U tests with significant differences ($P<0.01$) denoted by *

Differences between age groups were assed using a Kruscal Wallis test ($P=0.000$) with differences denoted by different superscript lower case letters

Vitamin K_1 intakes in 1-4y olds were different than 5-12 year olds ($P=0.000$) and 13-17 year olds ($P= 0.000$); Vitamin K_1 intakes in 5-12 year olds were different than 13-17 year olds ($P =0.000$)

Table 3. Contribution (µg & %) of food groups to the mean daily intake of vitamin K_1 in Irish pre-school children aged 1 to 4 years

	Total (*n* 500)		**1 year olds (*n* 126)**		**2 year olds (*n* 124)**		**3 year olds (*n* 126)**		**4 year olds (*n* 124)**	
Food Groups	**µg**	**%**	**µg**	**%**	**µg**	**%**	**µg**	**%**	**µg**	**%**
Vegetable & vegetable dishes	**11.7**	**26.3**	**12.3**	**25.6**	**9.5**	**23.1**	**10.5**	**25.1**	**14.4**	**31.3**
Green vegetables	*8.0*	*15.1*	*8.5*	*14.4*	*5.9*	*12.0*	*7.0*	*14.7*	*10.5*	*19.4*
Peas, beans & lentils	*1.0*	*3.4*	*1.1*	*3.2*	*0.9*	*3.3*	*0.9*	*3.2*	*1.1*	*3.7*
Other vegetables	*2.7*	*7.8*	*2.8*	*7.9*	*2.7*	*7.8*	*2.6*	*7.3*	*2.9*	*8.2*
Fruit & fruit juices	**5.0**	**17.5**	**4.9**	**16.9**	**5.0**	**18.8**	**5.5**	**18.6**	**4.5**	**15.7**
Grapes & berries	*1.5*	*5.6*	*1.3*	*5.1*	*1.5*	*6.0*	*2.0*	*6.5*	*1.3*	*4.7*
Fruit juices & purees	*0.9*	*3.4*	*1.1*	*4.0*	*1.0*	*3.5*	*1.0*	*3.6*	*0.7*	*2.4*
Other Fruits	*2.5*	*8.6*	*2.5*	*7.8*	*2.5*	*9.3*	*2.5*	*8.5*	*2.4*	*8.6*
Milks	**4.0**	**12.1**	**7.9**	**23.2**	**4.6**	**13.2**	**1.8**	**6.9**	**1.6**	**5.0**
Fortified infant & young child formula	*2.6*	*6.3*	*6.1*	*15.2*	*3.2*	*7.5*	*0.6*	*1.8*	*0.4*	*0.8*
Other milks	*1.4*	*5.7*	*1.8*	*7.9*	*1.4*	*5.7*	*1.2*	*5.1*	*1.1*	*4.2*
Meat & meat products	3.1	11.2	2.9	10.4	3.5	11.9	3.0	11.3	3.1	11.3
Butter, spreading fats & oils	1.6	6.1	0.9	3.5	1.7	7.0	1.9	7.6	1.8	6.5
Potatoes & potato products	1.3	5.4	0.9	3.9	1.3	5.0	1.6	6.6	1.5	6.0
Biscuits, cakes & pastries	1.3	4.8	1.1	3.8	1.2	4.3	1.2	5.0	1.7	5.9
Soups, sauces, & miscellaneous foods	1.0	3.2	0.6	2.1	1.2	3.5	0.9	3.3	1.2	3.8
Bread & rolls	0.6	2.3	0.3	1.3	0.6	2.6	0.7	2.7	0.7	2.6
Fish & fish dishes	0.6	2.0	0.5	1.7	0.4	1.5	0.6	2.3	0.7	2.3
Sugars, confectionery, preserves & savoury snacks	0.5	2.4	0.2	1.0	0.5	2.2	0.7	3.5	0.7	2.9
Breakfast cereals	0.5	2.0	0.7	2.6	0.5	2.1	0.4	1.7	0.4	1.7
Grains, rice, pasta and savouries	0.4	1.6	0.4	1.4	0.4	1.5	0.4	1.7	0.4	1.6
Cheese	0.3	1.3	0.3	1.1	0.3	1.4	0.3	1.3	0.4	1.3
Creams, ice-creams & chilled desserts	0.2	0.5	0.1	0.3	0.2	0.6	0.1	0.6	0.2	0.7
Yogurt & fromage frais	0.2	0.7	0.2	0.8	0.1	0.6	0.2	0.7	0.1	0.6
Eggs & egg dishes	0.1	0.4	0.1	0.3	0.1	0.5	0.1	0.4	0.1	0.3
Nuts seeds herbs & spices	0.1	0.3	0.1	0.2	0.0	0.2	0.1	0.6	0.1	0.2
Beverages	0.0	0.1	0.0	0.1	0.0	0.1	0.0	0.0	0.0	0.1
Total	**32.3**	**100**	**34.3**	**100**	**31.2**	**100**	**30.0**	**100**	**33.7**	**100**

Table 4. Contribution (µg & %) of food groups to the mean daily intake of vitamin K_1 in Irish children aged 5 to 12 years by age group

	All (*n* 594)		**5-8y (*n* 296)**		**9-12y (*n* 298)**	
Food Groups	**µg**	**%**	**µg**	**%**	**µg**	**%**
Vegetable & vegetable dishes	**16.0**	**29.3**	**15.5**	**30.0**	**16.5**	**28.6**
Green vegetables	*9.3*	*15.8*	*9.6*	*17.0*	*9.0*	*14.6*
Peas, beans & lentils	*1.5*	*4.3*	*1.7*	*4.8*	*1.4*	*3.8*
Vegetable & pulse dishes	*2.7*	*4.0*	*2.2*	*3.6*	*3.2*	*4.4*
Other vegetables	*2.5*	*5.2*	*2.0*	*4.7*	*2.9*	*5.7*
Potatoes & potato products	**4.9**	**15.0**	**4.2**	**13.7**	**5.7**	**16.3**
Chipped, fried & roasted products	*4.1*	*12.3*	*3.4*	*10.9*	*4.8*	*13.6*
Other potatoes and potato products	*0.9*	*2.7*	*0.9*	*2.8*	*0.9*	*2.7*
Meat & meat products	**4.0**	**11.4**	**3.4**	**10.9**	**4.5**	**11.8**
Meat products	*2.0*	*6.1*	*1.7*	*5.7*	*2.4*	*6.6*
Meat dishes	*1.8*	*4.8*	*1.7*	*4.9*	*1.9*	*4.8*
Other meats	*0.1*	*0.4*	*0.1*	*0.3*	*0.1*	*0.5*
Butter, spreading fats & oils	3.1	9.4	2.9	9.4	3.3	9.3
Fruit & fruit juices	2.8	7.4	3.0	8.6	2.5	6.3
Sugars, confectionery, preserves & savoury snacks	1.7	5.5	1.5	5.2	1.9	5.9
Milk & yoghurt	1.6	5.3	1.7	5.8	1.6	4.7
Biscuits, cakes & pastries	1.6	4.8	1.6	5.0	1.6	4.7
Soups, sauces & miscellaneous foods	1.0	2.5	0.8	2.3	1.1	2.7
Grains, rice, pasta and savouries	0.8	2.3	0.7	2.2	0.8	2.4
Bread & rolls	0.7	2.0	0.6	2.0	0.7	2.1
Breakfast cereals	0.4	1.3	0.4	1.3	0.4	1.2
Fish & fish dishes	0.4	1.0	0.4	1.1	0.4	0.9
Creams, ice-creams & chilled desserts	0.4	1.0	0.3	0.9	0.4	1.2
Cheese	0.2	0.8	0.2	0.8	0.3	0.8
Eggs & egg dishes	0.2	0.6	0.2	0.6	0.2	0.6
Beverages	0.1	0.3	0.1	0.2	0.1	0.4
Nuts, seeds, herbs & spices	0.1	0.2	0.1	0.2	0.1	0.2
Total	**39.9**	**100**	**37.6**	**100**	**42.1**	**100**

Table 5. Contribution (µg & %) of food groups to the mean daily intake of vitamin K_1 in Irish children aged 5 to 12 years by gender and age group

	Boys						**Girls**					
	All ages (*n* 291)		**5-8y (*n* 144)**		**9-12y (*n* 147)**		**All ages (*n* 303)**		**5-8y (*n* 152)**		**9-12y (*n* 151)**	
Food Groups	**µg**	**%**	**µg**	**%**	**µg**	**%**	**µg**	**%**	**µg**	**%**	**µg**	**%**
Vegetable & vegetable dishes	**15.5**	**28.1**	**14.2**	**28.6**	**16.8**	**27.6**	**16.4**	**30.5**	**16.7**	**31.4**	**16.1**	**29.6**
Green vegetables	*9.3*	*15.8*	*9.5*	*17.2*	*9.1*	*14.4*	*9.3*	*15.8*	*9.6*	*16.7*	*9.0*	*14.9*
Peas, beans & lentils	*1.8*	*4.8*	*2.0*	*5.6*	*1.5*	*4.1*	*1.3*	*3.7*	*1.4*	*4.0*	*1.2*	*3.5*
Vegetable & pulse dishes	*2.3*	*3.0*	*1.1*	*1.8*	*3.6*	*4.2*	*3.0*	*5.0*	*3.2*	*5.3*	*2.8*	*4.7*
Other vegetables	*2.1*	*4.4*	*1.6*	*4.0*	*2.6*	*4.9*	*2.8*	*5.9*	*2.5*	*5.4*	*3.1*	*6.5*
Potatoes & potato products	**5.2**	**15.4**	**4.6**	**14.4**	**5.8**	**16.5**	**4.7**	**14.6**	**3.9**	**13.0**	**5.6**	**16.1**
Chipped, fried & roasted products	*4.3*	*12.8*	*3.7*	*11.5*	*4.9*	*14.0*	*3.8*	*11.8*	*3.1*	*10.4*	*4.6*	*13.2*
Other potatoes and potato products	*0.8*	*2.6*	*0.9*	*2.9*	*0.8*	*2.4*	*0.9*	*2.8*	*0.8*	*2.7*	*1.0*	*2.9*
Meat & meat products	**4.1**	**11.5**	**3.6**	**11.5**	**4.5**	**11.6**	**3.8**	**11.2**	**3.3**	**10.3**	**4.4**	**12.1**
Meat products	*2.1*	*6.4*	*1.9*	*6.5*	*2.4*	*6.3*	*1.9*	*5.9*	*1.5*	*4.9*	*2.4*	*6.8*
Meat dishes	*1.8*	*4.8*	*1.6*	*4.6*	*2.0*	*4.9*	*1.8*	*4.9*	*1.7*	*5.1*	*1.9*	*4.7*
Other meats	*0.1*	*0.4*	*0.1*	*0.4*	*0.1*	*0.4*	*0.1*	*0.4*	*0.1*	*0.3*	*0.1*	*0.5*
Butter, spreading fats & oils	3.4	9.8	3.2	10.0	3.6	9.7	2.8	8.9	2.7	8.9	3.0	8.9
Fruit & fruit juices	2.6	7.2	2.9	8.5	2.3	5.9	2.9	7.6	3.1	8.6	2.7	6.6
Sugars, confectionery, preserves & savoury snacks	1.7	5.5	1.5	5.0	1.9	5.9	1.7	5.6	1.5	5.4	1.9	5.8
Biscuits, cakes & pastries	1.6	5.1	1.6	5.3	1.6	4.9	1.6	4.6	1.6	4.6	1.6	4.5
Milk & yoghurt	1.8	5.7	1.7	5.9	1.8	5.6	1.4	4.8	1.6	5.6	1.3	3.9
Soups, sauces & miscellaneous foods	0.7	1.9	0.5	1.5	0.9	2.2	1.2	3.1	1.2	3.0	1.3	3.1
Grains, rice, pasta and savouries	0.7	2.2	0.5	1.8	0.9	2.7	0.8	2.3	0.8	2.5	0.8	2.2
Bread & rolls	0.7	2.2	0.7	2.1	0.7	2.2	0.6	1.9	0.6	1.8	0.7	2.0
Breakfast cereals	0.5	1.5	0.4	1.5	0.5	1.6	0.3	1.0	0.3	1.1	0.3	0.9
Fish & fish dishes	0.4	1.1	0.4	1.3	0.4	0.9	0.4	0.9	0.4	0.9	0.4	1.0
Creams, ice-creams & chilled desserts	0.3	0.9	0.3	1.0	0.3	0.9	0.4	1.2	0.3	0.9	0.5	1.4
Cheese	0.2	0.7	0.2	0.6	0.3	0.7	0.3	0.8	0.3	0.9	0.3	0.8
Eggs & egg dishes	0.2	0.6	0.2	0.5	0.3	0.7	0.2	0.6	0.2	0.6	0.2	0.5
Beverages	0.1	0.3	0.1	0.2	0.1	0.4	0.1	0.3	0.1	0.2	0.1	0.4
Nuts, seeds, herbs & spices	0.1	0.2	0.1	0.2	0.1	0.2	0.1	0.2	0.1	0.2	0.1	0.3
Total	**39.8**	**100**	**36.7**	**100**	**42.8**	**100**	**39.9**	**100**	**38.6**	**100**	**41.3**	**100**

Table 6. Contribution (µg & %) of food groups to the mean daily intake of vitamin K_1 in Irish teenagers aged 13 to 17 years by age group

	All (*n* 441)		13-14y (*n* 188)		15-17y (*n* 253)	
Food groups	**µg**	**%**	**µg**	**%**	**µg**	**%**
Vegetable & vegetable dishes	**23.0**	**32.3**	**23.4**	**33.2**	**22.8**	**31.7**
Green vegetables	*11.6*	*14.6*	*13.5*	*16.8*	*10.1*	*13.1*
Salad vegetables	*3.7*	*5.9*	*2.9*	*5.0*	*4.2*	*6.6*
Other vegetables	*7.8*	*11.8*	*6.9*	*11.4*	*8.4*	*12.1*
Potatoes & potato products	**7.9**	**16.9**	**7.8**	**17.5**	**8.0**	**16.5**
Chipped, fried & roasted potatoes	*6.5*	*14.1*	*6.4*	*14.6*	*6.5*	*13.7*
Other potatoes & potato products	*1.4*	*2.8*	*1.4*	*2.9*	*1.4*	*2.8*
Meat & meat products	**6.2**	**13.2**	**6.2**	**13.2**	**6.2**	**13.2**
Meat dishes	*2.5*	*5.4*	*2.3*	*5.0*	*2.7*	*5.7*
Meat products	*2.0*	*4.2*	*2.1*	*4.1*	*1.9*	*4.2*
Other meats	*1.7*	*3.7*	*1.8*	*4.1*	*1.6*	*3.3*
Butter, spreading fats & oils	4.0	8.4	4.0	8.8	4.1	8.2
Soups, sauces & miscellaneous foods	2.4	4.7	1.8	3.6	2.9	5.4
Sugars, confectionery, preserves & savoury snacks	1.9	4.6	1.9	4.8	1.9	4.4
Fruit & fruit juices	2.2	4.1	2.0	3.9	2.4	4.3
Milk & yoghurt	1.4	3.1	1.4	3.1	1.4	3.1
Biscuits, cakes & pastries	1.4	2.8	1.2	2.7	1.4	2.8
Grains, rice, pasta and savouries.	1.3	2.8	1.1	2.4	1.4	3.0
Bread & rolls	0.8	1.8	0.7	1.6	1.0	1.9
Fish & fish dishes	0.6	1.1	0.6	1.2	0.6	1.0
Breakfast cereals	0.4	1.0	0.4	0.9	0.5	1.0
Cheese	0.5	1.0	0.4	1.0	0.5	0.9
Beverages	0.3	0.7	0.2	0.6	0.3	0.8
Creams, ice-creams & chilled desserts	0.4	0.7	0.3	0.7	0.4	0.8
Eggs & egg dishes	0.3	0.5	0.3	0.5	0.2	0.5
Nuts, seeds, herbs & spices	0.2	0.3	0.2	0.3	0.2	0.3
Total	**55.2**	**100**	**53.9**	**100**	**56.1**	**100**

Table 7. Contribution (µg & %) of food groups to the mean daily intake of vitamin K_1 in Irish teenagers aged 13 to 17 years by gender and age group

	Boys						**Girls**					
	All ages (*n* 224)		**13-14y (*n* 94)**		**15-17y (*n* 130)**		**All ages (*n* 217)**		**13-14y (*n* 94)**		**15-17y (*n* 123)**	
Food groups	**µg**	**%**	**µg**	**%**	**µg**	**%**	**µg**	**%**	**µg**	**%**	**µg**	**%**
Vegetable & vegetable dishes	**24.4**	**31.2**	**25.5**	**33.9**	**23.6**	**29.2**	**21.6**	**33.5**	**21.2**	**32.4**	**21.9**	**34.4**
Green vegetables	*12.9*	*15.0*	*15.1*	*18.1*	*11.2*	*12.8*	*10.3*	*14.2*	*12.0*	*15.5*	*9.0*	*13.3*
Salad vegetables	*3.4*	*4.8*	*3.1*	*4.4*	*3.6*	*5.0*	*4.0*	*7.1*	*2.8*	*5.6*	*4.9*	*8.2*
Other vegetables	*8.2*	*11.4*	*7.3*	*11.5*	*8.8*	*11.3*	*7.4*	*12.2*	*6.5*	*11.3*	*8.0*	*12.9*
Potatoes & potato products	**8.6**	**16.7**	**8.4**	**17.0**	**8.8**	**16.5**	**7.2**	**17.1**	**7.2**	**17.9**	**7.1**	**16.5**
Chipped, fried & roasted products	*7.0*	*13.6*	*6.7*	*13.6*	*7.2*	*13.6*	*6.0*	*14.6*	*6.1*	*15.6*	*5.9*	*13.8*
Other potatoes & potato products	*1.7*	*3.1*	*1.7*	*3.3*	*1.6*	*3.0*	*1.2*	*2.5*	*1.1*	*2.3*	*1.2*	*2.7*
Meat & meat products	**7.2**	**14.5**	**6.9**	**12.9**	**7.5**	**15.6**	**5.1**	**12.0**	**5.5**	**13.5**	**4.8**	**10.8**
Meat dishes	*3.1*	*6.1*	*2.7*	*5.0*	*3.4*	*6.9*	*2.0*	*4.7*	*2.0*	*4.9*	*1.9*	*4.5*
Meat products	*2.5*	*5.0*	*2.6*	*4.7*	*2.4*	*5.2*	*1.5*	*3.3*	*1.6*	*3.6*	*1.4*	*3.1*
Other meats	*1.7*	*3.4*	*1.6*	*3.2*	*1.8*	*3.5*	*1.7*	*4.0*	*2.0*	*5.1*	*1.4*	*3.2*
Butter, spreading fats & oils	4.7	9.3	4.9	9.7	4.6	9.0	3.3	7.6	3.1	7.9	3.5	7.4
Soups, sauces & miscellaneous foods	2.3	3.8	1.5	2.7	2.9	4.6	2.6	5.6	2.2	4.6	2.9	6.3
Sugars, confectionery, preserves & savoury snacks	1.8	4.1	1.8	4.2	1.8	4.0	2.0	5.1	2.1	5.4	2.0	4.8
Fruit & fruit juices	2.2	3.5	1.9	3.2	2.4	3.8	2.3	4.7	2.0	4.6	2.5	4.8
Milk & yoghurt	1.8	3.8	1.8	4.0	1.8	3.8	1.0	2.4	0.9	2.2	1.1	2.5
Biscuits, cakes & pastries	1.5	2.8	1.3	2.5	1.7	3.1	1.2	2.7	1.2	2.9	1.2	2.6
Grains, rice, pasta and savouries	1.4	2.7	1.4	2.5	1.5	2.9	1.2	2.8	0.9	2.3	1.3	3.1
Bread & rolls	0.9	1.8	0.7	1.5	1.1	1.9	0.8	1.8	0.6	1.6	0.9	1.9
Fish & fish dishes	0.7	1.2	0.7	1.4	0.6	0.9	0.6	1.0	0.5	0.9	0.6	1.1
Breakfast cereals	0.6	1.2	0.5	1.1	0.6	1.3	0.3	0.7	0.3	0.7	0.3	0.8
Cheese	0.5	1.0	0.4	0.8	0.6	1.1	0.4	1.0	0.5	1.1	0.4	0.8
Beverages	0.3	0.7	0.3	0.5	0.4	0.8	0.3	0.7	0.2	0.7	0.3	0.8
Creams, ice-creams & chilled desserts	0.4	0.7	0.4	0.8	0.4	0.7	0.3	0.7	0.3	0.6	0.4	0.8
Eggs & egg dishes	0.3	0.6	0.4	0.6	0.3	0.6	0.2	0.5	0.2	0.4	0.2	0.5
Nuts, seeds, herbs & spices	0.2	0.4	0.3	0.5	0.2	0.4	0.1	0.2	0.1	0.2	0.1	0.2
Total	**59.8**	**100**	**58.7**	**100**	**60.6**	**100**	**50.5**	**100**	**49.1**	**100**	**51.5**	**100**

Discussion

The aim of this chapter was to estimate the mean daily intake and key dietary sources of vitamin K_1 in Irish children aged 1-17 years across three nationally representative dietary surveys of children in Ireland. The key finding was that vitamin K_1 intake was generally above the AI of 1µg/kg/d proposed by EFSA with 'vegetable & vegetable dishes' the key source of vitamin K_1 in all gender and age groups.

Based on the role of vitamin K in blood coagulation, EFSA have set an AI of 1µg/kg/d for all gender and age groups (EFSA Panel on Dietetic Products *et al.*, 2017). Recent studies have suggested a role of vitamin K beyond its traditional role in blood coagulation in functions such as bone health, cardiovascular health, and cognition and anti-inflammatory functions in adults (Booth, 2009, Vermeer, 2012, Halder *et al.*, 2019). In addition, it has been demonstrated that a better vitamin K status is associated with decreased bone turnover (Kalkwarf et al., 2004) and an increase in bone mineral content in children (O'Connor *et al.*, 2007, Van Summeren *et al.*, 2008).

Vitamin K_1 intake in Irish children at age 1-4 years was above the AI of 1µg/kg/d (Age 1: 3.0µg/kg/d, age 2: 2.3µg/kg/d, age 3 & 4: 1.8µg/kg/d). Vitamin K_1 intake in 4 year old Irish children were compared to the intake reported by Prynne *et al.* (2005) in 4 year old children from Britain. The cross-sectional National Diet and Nutrition Surveys (1992/93 and 1997) used a 4-day (1992/93) and 7-day (1997) weighed dietary record to estimate vitamin K_1 intake. Intakes were 1.4µg/kg/d (average across the two surveys) for British children aged 4 years in the 1990s, which is lower than intakes reported in Irish children of the same age.

The Genesis study (2003-2004) aimed to assess the nutrient adequacy of a representative sample (*n* 2,374) of toddlers and pre-school children aged 1-5 years in Greece using dietary data collected via a 3-day weighed food record (Manios *et al.*, 2008). Usual intakes of vitamin K (assumed to be vitamin K_1) were 32.2µg/d which is similar to the 32.3µg/d found in the NPNS from age 1-4 years.

For Irish children aged 5-12 years, intakes of vitamin K_1 were above the AI of 1µg/kg/d (5-8 years; 1.5 µg/kg/d, 9-12 years; 1.1 µg/kg/d). There were no difference in intakes between boys and girls. Vitamin K_1 intakes in teenagers aged 13-17 years were less than the AI of 1µg/kg/d with the exception of younger boys aged 13-14 years. In general, intakes in Irish children and teenagers in this study were lower than intakes reported in national surveys in Austrian and American children. The Austrian dietary survey (2010-2012) used a 3-day dietary record to estimate food and beverage intakes in 163 girls and 169 boys aged 7 to 14 years (Elmadfa *et al.*, 2012). Vitamin K_1 intakes were 67 and 74µg per day for Austrian boys and girls aged 7-9 years, respectively. These findings are higher than intakes reported in the Irish NCFS (5-8 year olds; 37.6µg/d, 9-12 year olds; 42.1µg/d). Vitamin K_1 intakes at age 13-14 years in Austria were 69 and 61µg/d in boys and girls aged 13-14 years, respectively, versus 49.1 and 58.7µg/d in boys and girls of the same age in the Irish NTFS, respectively.

Vitamin K_1 intakes were reported for children and teenagers in the National Health and Nutrition Examination Survey (NHANES) (2015-2016); a national food survey in America (US Department of Agriculture, 2018). Intakes in American children at age 2-5 years, 6-11 years and 12-19 years were 48-55, 63 and 74-79µg/d, respectively. Although there are differences in the age categories between NHANES and the Irish data, in general, vitamin K_1 intakes are higher in American children.

Across all survey groups, 'vegetable & vegetable dishes' was the key source of vitamin K_1 intake (26-32%). Of this, 'green vegetables' accounted for 15-16% of intake. 'Fruit & fruit juices' was the second highest contributor to the MDI of vitamin K_1 in pre-school children with a contribution of 5µg (18% of total intake). Fruit & fruit juices' only contributed 4-9% of total vitamin K_1 intake in older age groups (5-12 years; 13-17 years). The difference is attributable to the higher consumption of 'fruit & fruit juices' in Irish pre-school children (132g-198g) compared to the older age groups (148-162g). Fruit juices typically do not contain vitamin K_1; therefore, the contribution from the 'fruit & fruit juices' food group is coming from the consumption of whole fruits some of which contain moderate amounts of vitamin K_1 such as green fruits and berries (Dismore *et al.*, 2003).

For pre-school children (1-4 years), the contribution of vitamin K_1 from 'milks' was 23% at age 1 year with 'fortified infant and young child formula' accounting for 15% of intakes. The typical vitamin K composition of infant and child formulae consumed on the NPNS were 4-10µg vitamin K per 100ml. No other milks other than 'infant and young child formula' were fortified with vitamin K. According to EFSA, intakes of 12 µg per day are deemed adequate to meet the vitamin K needs of infants 12 to <36 months, (EFSA Panel on Dietetic Products and Allergies, 2013) and it is recommended that all infant and follow on formulas are fortified with vitamin K to a minimum level of 1µg/100kcal (EFSA Panel on Dietetic Products and Allergies, 2014) to ensure normal blood coagulation of the infant.

For older children and teenagers, ‘potatoes & potato products’ was the second highest contributor to the MDI of vitamin K_1 (15-17%). It is important to note that this is predominantly from ‘chipped, fried & roasted products’ (12-14%) due to the oils used in their preparation and cooking. Some vegetable and seed oils are considered to be one of the few food categories high in vitamin K_1 (Peterson *et al.*, 2002). Examples of oils high in vitamin K_1 include olive oil (57.5µg/100g) and blended vegetable oil (114.4µg/100g); however, sunflower (6.3µg/100g) and corn oil (3 µg/100g) are considered low in vitamin K_1. Thus, the vitamin K_1 content of certain foods cooked or produced with oils will vary depending on the type of oils used in its preparation. This study accounted for the use of different oils in food preparation and cooking due to the ability to separate recipes at an ingredient level. The vitamin K_1 content of oils can also be variable depending on light exposure, storage conditions and also within brands (Ferland and Sadowski, 1992, Peterson *et al.*, 2002).

Few studies have investigated the sources of vitamin K_1 in children. Prynne *et al.* (2005) reported that ‘vegetable and vegetable products’ contributed 48% of vitamin K_1 intake in British children aged 4 years, of which, 15% came from ‘green leafy vegetables’. Intakes (g/d) of vegetables in British children and Irish children were 125g/d and 60g/d, respectively, which may explain the higher contribution from vegetables in the British children. ‘Potato and potato products’ accounted for 18% of intakes in British children which is far higher than the 6% contribution in the Irish children at age 4 years. Variances in the foods included in the ‘potato and potato products’ may partly explain the large difference considering that crisps were included in this food category in the study by Prynne *et al.* (2005). Additional foods may have been included that are not outlined. Similarly, data from the Food and Drug Administrations Total Diet Study in the US (1987-88) reported that green vegetables were the top contributor to vitamin K_1 intake (26-35%) across each gender and age group from 2-16 years (Booth *et al.*, 1996).

Strengths and limitations

The main strengths of the present study were the high quality dietary data available to conduct our analysis (including brand level detail) and the use of nationally representative data for estimating vitamin K_1 intake and adequacy. Furthermore, the detailed methodology used to assign vitamin K_1 values to each food consumed is a great strength of this study (chapter 3). Each recipe consumed across the three surveys were individually analysed to account for the different types of oils and vegetables used in mixed dishes which has a significant influence on vitamin K_1 content. Although under reporting of food consumption is an issue with dietary assessment especially in children and adolescents, this was minimised across the three surveys by high levels of interaction with trained researchers over the food diary recording period.

Conclusions

This study will add to the small pool of data examining vitamin K_1 intake in children and is the first of its kind to report the intake and key dietary sources of vitamin K_1 in nationally representative samples of Irish children and teenagers. Vitamin K_1 intake in preschool (1-4 years) and school-aged children (5-12 years) were above the AI of 1µg/kg/d. However, vitamin K_1 intake in teenagers was less than the AI with the exception of younger boys aged 13-14 years. 'Vegetable & vegetable dishes' was consistently the highest contributor to vitamin K_1 intake across all gender and age groups in the three surveys. There was a steady increase in the contribution from this food group with increasing age across each survey (1-4 years; 26%, 5-12 years; 29%, 13-17 years; 32%). 'Fruit & fruit juices' was the second highest contributor to vitamin K_1 intake from age 1-4 years (16%-19%). The contribution from 'milks' decreased significantly with increasing age from age 1 year to age 3-4 years primarily due to consumption of 'fortified infant and young child formula' in the earlier years. 'Potatoes & potato products' was also an important source of vitamin K_1 in the older age groups (5-12 years & 13-17 years) (15-17%). Of this, 'chipped, fried & roasted products' accounted for between 12-14% of vitamin K_1 intake predominantly due to the oils used in their preparation and cooking. Further investigation is necessary to fully understand the role of vitamin K in overall health in children and teenagers and the implications of long-term lower vitamin K status throughout childhood.

References

Bolton-Smith, C., Price, R. J., Fenton, S. T., Harrington, D. J. & Shearer, M. J. (2000). Compilation of a provisional UK database for the phylloquinone (vitamin K1) content of foods. *British Journal of Nutrition*, 83**,** 389-99.

Booth, S. L. (2009). Roles for vitamin K beyond coagulation. *The Annual Review of Nutrition*, 29**,** 89-110.

Booth, S. L., Pennington, J. A. & Sadowski, J. A. (1996). Food sources and dietary intakes of vitamin K-1 (phylloquinone) in the American diet: data from the FDA Total Diet Study. *Journal of the American Dietetic Association,* 96**,** 149-54.

Booth, S. L., Sadowski, J. A., Weihrauch, J. L. & Ferland, G. (1993). Vitamin K1 (Phylloquinone) Content of Foods: A Provisional Table. *Journal of Food Composition and Analysis,* 6**,** 109-120.

Damon, M., Zhang, N. Z., Haytowitz, D. B. & Booth, S. L. (2005). Phylloquinone (vitamin K1) content of vegetables. *Journal of Food Composition and Analysis,* 18**,** 751-758.

Dismore, M. L., Haytowitz, D. B., Gebhardt, S. E., Peterson, J. W. & Booth, S. L. (2003). Vitamin K content of nuts and fruits in the US diet. *Journal of the American Dietetic Association,* 103**,** 1650-2.

EFSA Panel on Dietetic Products, N. & Allergies (2013). Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union. *EFSA Journal,* 11**,** 3408.

EFSA Panel on Dietetic Products, N. & Allergies (2014). Scientific Opinion on the essential composition of infant and follow-on formulae. *EFSA Journal,* 12**,** 3760.

EFSA Panel on Dietetic Products, N., Allergies, Turck, D., Bresson, J.-L., Burlingame, B., Dean, T., Fairweather-Tait, S., Heinonen, M., Hirsch-Ernst, K. I., Mangelsdorf, I., McArdle, H. J., Naska, A., Nowicka, G., Pentieva, K., Sanz, Y., Siani, A., Sjödin, A., Stern, M., Tomé, D., Van Loveren, H., Vinceti, M., Willatts, P., Lamberg-Allardt, C., Przyrembel, H., Tetens, I., Dumas, C., Fabiani, L., Ioannidou, S. & Neuhäuser-Berthold, M. (2017). Dietary reference values for vitamin K. *EFSA Journal*, 15**,** e04780.

Elmadfa, I., Hasenegger, V., Wagner, K., Putz, P., Weidl, N.-M., Wottawa, D., Kuen, T., Seiringer, G., Meyer, A., Sturtzel, B., Kiefer, I., Zilberszac, A., Sgarabottolo, V., Meidlinger, B. & Rieder, A. (2012). Österreichischer Ernährungsbericht 2012.

Fagerland, M. W. (2012). t-tests, non-parametric tests, and large studies—a paradox of statistical practice? *BMC Medical Research Methodology,* 12**,** 78.

Ferland, G. & Sadowski, J. A. (1992). Vitamin K1 (phylloquinone) content of edible oils: effects of heating and light exposure. *Journal of Agricultural and Food Chemistry,* 40**,** 1869-1873.

Food Standards Agency (2002). Food Portion Sizes. London: The Stationary Office.

Foster., E., Hawkins A & Adamson A 2010. *Young Person's Food Atlas: Pre-school. London, Food Standards Agency.*

Halder, M., Petsophonsakul, P., Akbulut, A. C., Pavlic, A., Bohan, F., Anderson, E., Maresz, K., Kramann, R. & Schurgers, L. (2019). Vitamin K: Double Bonds beyond Coagulation Insights into Differences between Vitamin K1 and K2 in Health and Disease. *International Journal of Molecular Sciences,* 20**,** 896.

Hannon, E. M., Cashman, K., Kiely, M. & Flynn, A. (2007). Phylloquinone intakes and food sources in Irish children aged 5-12 years. *Proceedings of the Nutrition Society,* 66**,** 32A-114A.

Hayes, A., Hennessy, A., Walton, J., McNulty, B. A., Lucey, A. J., Kiely, M., Flynn, A. & Cashman, K. D. (2016). Phylloquinone Intakes and Food Sources and Vitamin K Status in a Nationally Representative Sample of Irish Adults. *Journal of Nutrition,* 146**,** 2274-2280.

Krebs-Smith, S. M., Kott, P. S. & Guenther, P. M. (1989). Mean proportion and population proportion: two answers to the same question? *Journal of the American Dietetic Association,* 89**,** 671-6.

Lyons, J., Walton, J. & Flynn, A. (2013). Development of an online database of typical food portion sizes in Irish population groups. *Journal of nutritional science,* 2**,** e25-e25.

Manios, Y., Grammatikaki, E., Papoutsou, S., Liarigkovinos, T., Kondaki, K. & Moschonis, G. (2008). Nutrient intakes of toddlers and preschoolers in Greece: the GENESIS study. *Journal of the American Dietetic Association,* 108**,** 357-61.

Nelson., M., Atkinson M & Meyer J (1997). A photographic atlas of food portion sizes. England: Food Standards Agency.

O'Connor, E., Molgaard, C., Michaelsen, K. F., Jakobsen, J., Lamberg-Allardt, C. J. & Cashman, K. D. (2007). Serum percentage undercarboxylated osteocalcin, a sensitive measure of vitamin K status, and its relationship to bone health indices in Danish girls. *British Journal of Nutrition,* 97**,** 661-6.

Peterson, J. W., Muzzey, K. L., Haytowitz, D., Exler, J., Lemar, L. & Booth, S. L. (2002). Phylloquinone (vitamin K1) and dihydrophylloquinone content of fats and oils. *Journal of the American Oil Chemists' Society,* 79**,** 641-646.

Presse, N., Potvin, S., Bertrand, B., Calvo, M. S. & Ferland, G. (2015). Phylloquinone content of herbs, spices and seasonings. *Journal of Food Composition and Analysis,* 41**,** 15-20.

Prynne, C. J., Thane, C. W., Prentice, A. & Wadsworth, M. E. (2005). Intake and sources of phylloquinone (vitamin K(1)) in 4-year-old British children: comparison between 1950 and the 1990s. *Public Health Nutrition,* 8**,** 171-80.

Public Health England Composition of Foods Integrated Dataset. 2015. *McCance and Widdowson's The Composition of Foods Integrated Dataset 2015* [Online]. Available: https://www.gov.uk/government/publications/composition-of-foods-integrated-dataset-cofid.

US Department of Agriculture (2018). Nutrient Intakes from Food and Beverages: Mean amounts consumed per Individual , by Gender and Age, What we eat in America, NHANES 2015-2016.

USDA National Nutrient Database for Standard References Release 28. 2015. Washington (DC): USDA Agricultural Research Service. Available: http://www.ars.usda.gov/nutrientdata [Accessed January 2016].

Van Summeren, M. J., van Coeverden, S. C., Schurgers, L. J., Braam, L. A., Noirt, F., Uiterwaal, C. S., Kuis, W. & Vermeer, C. (2008). Vitamin K status is associated with childhood bone mineral content. *British Journal of Nutrition,* 100**,** 852-8.

Vermeer, C. (2012). Vitamin K: the effect on health beyond coagulation – an overview. *Food & Nutrition Research,* 56**,** 10.3402/fnr.v56i0.5329.

Chapter 5

Intakes and sources of vitamin K_2 (menaquinones) in the Irish population aged 1 to 90 years

Tentative title: Intakes of vitamin K_2 in the Irish population aged 1-90 years

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Introduction

Menaquinones or vitamin K_2 are a biologically active form of vitamin K that contain side chains of varying length typically between 4 and 13 isoprene units. Menaquinones are synthesized by bacteria with the exception of menaquinone-4; which is formed from the tissue specific conversion from dietary phylloquinone or menadione present in animal feed (Dialameh *et al.*, 1971, Okano *et al.*, 2008, EFSA Panel on Additives and Products or Substances used in Animal Feed, 2014). The longer chained menaquinones (menaquinone-5-10) are synthesised by bacteria including bacteria that function in food fermentation. Fermentation conditions and the starter culture used influence the concentration and type of menaquinones present in the food product (Walther *et al.*, 2013). Intestinal bacteria also produce menaquinones however, their contribution to vitamin K nutrition in the body is not yet fully understood (Conly *et al.*, 1994, Suttie, 1995, Karl *et al.*, 2017).

Due to its bacterial origin, vitamin K_2 is found in fermented food products and foods of animal origin such as meat, eggs and dairy and may account for up to 25% of total vitamin K intake (Schurgers and Vermeer, 2000, Elder *et al.*, 2006, Ferreira, 2006, Fu *et al.*, 2016, Fu *et al.*, 2017). Although vitamin K_1 is the predominant form of vitamin K in the human diet, the bioavailability of vitamin K_2 has been shown to be far higher than that of its vitamin K_1 counterpart (Schurgers and Vermeer, 2000, Schurgers and Vermeer, 2002, Schurgers *et al.*, 2007).

Studies investigating menaquinone intakes in adults and their association with specific health outcomes globally have reported that menaquinones may be important for bone health, cardiovascular health and cognition with intakes typically ranging from 12-35μg/d (Schurgers *et al.*, 1999, Geleijnse *et al.*, 2004, Nimptsch *et al.*, 2008, Beulens *et al.*, 2009, Gast *et al.*, 2009, Apalset *et al.*, 2010, Beulens *et al.*, 2010, Nimptsch *et al.*, 2010, Apalset *et al.*, 2011, Vissers *et al.*, 2013, McCann *et al.*, 2019). Despite this, the European Food Safety Authority (EFSA) has stated that there is still insufficient evidence on the function, bioavailability and content of menaquinones in the body to set a dietary reference value for vitamin K_2 (EFSA Panel on Dietetic Products *et al.*, 2017).

The Irish Food Composition Database (IFCD) (2012) is a database of all food and beverages consumed by the Irish population from four nationally representative dietary surveys. The IFCD (2012) has recently been updated to include menaquinone composition data (chapter 3). This chapter aims to use these data to estimate the intakes and key dietary sources of menaquinones (menaquinone-4 (MK-4) & menaquinone-5-10 (MK-5-10)) in the Irish population aged 1-90 years.

Methodology

The analysis for this chapter is based on data from four nationally representative dietary surveys of the Irish population; the National Pre-school Nutrition Survey (NPNS) of 1-4 year olds (2010-11), the National Children's Food Survey (NCFS) of 5-12 year olds (2003-04), the National Teens' Food Survey (NTFS) of 13-17 year olds (2005-06) and the National Adult Nutrition Survey (NANS) of 18-90 year olds (2008-10) (www.iuna.net). The methodology for sampling, participant recruitment, data collection and food quantification for these surveys is described in chapter 2. The methods used when updating the menaquinone content of foods in the IFCD (2012) are outlined in detail in chapter 3. Methods specific to this chapter are outlined below.

Food intake data collection and quantification

Food and beverage intake data were estimated for 500 pre-school children aged 1-4 years in the NPNS using a 4-day weighed food record. The fieldworker visited each participant 3 times over the recording period. For the NCFS, 594 children aged 5-12 years completed a 7-day weighed food record with a total of four visits from the fieldworker over the recording period. Similarly, 441 teenagers aged 13-17 years completed the NTFS using a 7-day semi-weighed food record with four visits from the fieldworker over the recording period. Fifteen hundred adults aged 18-90 years participated in the NANS, which collected dietary data using a 4-day semi weighed food record. Each participant was visited 3 times over the recording period.

For each survey, detailed information relating to the amount, type, cooking method, leftovers, packaging and brand of all foods and beverages (including nutritional supplements) consumed over the recording period was collected. Details of recipes of composite dishes were also recorded.

All food and beverage items consumed across the four surveys were quantified via one of the following methods; weighed (using the digital food scales provided to each participant), age appropriate photographic food atlases (Nelson. *et al.*, 1997, Foster. *et al.*, 2010), standard portion weights (Food Standards Agency, 2002, Lyons *et al.*, 2013) and household measures (such as teaspoon, tablespoon, pint etc).

Data entry

Each food and beverage consumed was assigned a unique food code depending on its nutritional profile. Dietary data were then entered into the data entry system WISP© (Tinuviel Software, Anglesey, UK). A separate database (food file) was created for each survey with one line of data for each food and drink item consumed.

Quality control

A number of quality procedures were put in place in an attempt to minimise error and ensure consistency throughout the collection and data entry of food intake. Each fieldworker was primarily responsible for the collection, quantification, coding and data entry of their own participants' food diaries in an attempt to maintain consistency.

Menaquinone composition data

As described in Chapter 3, each food code was assigned both a MK-4 and a MK-5-10 composition value using data from the UK Composition Of Foods Integrated Dataset (COFID) (Public Health England Composition of Foods Integrated Dataset, 2015), published papers (Schurgers and Vermeer (2000), Fu *et al.* (2016)), manufacturers' information and recipe calculation.

Statistical analyses

Statistical analyses were carried out using SPSS© for Windows™ Version 22.0. The Mean Daily Intake (MDI) of menaquinones were estimated and differences in intakes between gender and age groups were assessed using independent sample T-tests regardless of normality (due to the large sample size). As sample size increases so does the robustness of t-tests to identify deviations from normality, thus parametric tests are recommended for large samples (Fagerland, 2012). To minimise type 1 errors (as a result of multiple testing), the Bonferoni adjustment was used by dividing the alpha level (0.005) by the number of comparisons. Therefore, intakes were considered to be significantly different from each other if $P<0.001$. All data were not normally distributed. The non-parametric Kruskal- Wallis test was used to determine significant differences between independent groups. Where significant differences were identified by the Kruskal- Wallis test, the Mann Whitney U test was used to identify where these differences occurred.

To estimate the key dietary sources of menaquinones, all food and drinks consumed were allocated to one of nineteen food groups (Appendix I) and then further subdivided into 68 food groups (NCFS, NTFS & NANS) or 77 food groups (NPNS) (Appendix II). The percent contribution of each food group to the mean daily intake of menaquinones was calculated by the mean proportion method (Krebs-Smith *et al.*, 1989) and the key contributors to intakes were determined in order of importance for each age group. This method provides information about the sources that are contributing to the nutrient intake 'per person' and is the preferred method when determining important food sources of a nutrient for individuals in the population group as opposed to investigating the sources of a nutrient within the food supply.

Results

The mean daily intake of total MK (MK-4-10)

Tables 1 and 2 report the mean daily intake of total MK (MK-4-10) (µg/d & µg/10MJ) in the Irish population aged 1 to 90 years split by gender and age group. The Mean Daily Intake (MDI) of total MK in pre-school children aged 1-4 years and children aged 5-12 years was 40.1 and 51.8µg/d, respectively. Teenagers aged 13-17 years had a MDI of total MK of 55.3µg/d. Irish adults aged 18-64 years and 65-90 years had a MDI of total MK of 58.1 and 42.3µg/d, respectively.

The MDI of total MK was similar among children aged 5-12 years, teenagers aged 13-17 years and adults aged 18-64 years however, these intakes were higher than intakes in pre-school children aged 1-4 years and older adults aged 65-90 years. At ages 13-17 and 18-64 years, males had significantly higher intakes than females.

When intakes were adjusted for energy (µg/10MJ), pre-school children aged 1-4 years had a similar intake to children and teenagers aged 5-17 years and adults aged 18-64 years and and a higher intake than older adults aged 65-90 years, highlighting the nutrient dense diet consumed by young children. Energy adjusted intakes were similar between males and females of all ages with the exception of males aged 18-64 years having higher intakes than females due to males consuming a more MK-4-10 nutrient dense diet.

The mean daily intake of MK-4

Tables 3 and 4 report the mean daily intake of MK-4 (µg/d & µg/10MJ) in the Irish population aged 1 to 90 years split by gender and age group. The MDI of MK-4 in pre-school children aged 1-4 years was 7.7µg/d. The MDI of MK-4 was 10.1µg/d in Irish children aged 5-12 years and 12.3µg/d in teenagers aged 13-17 years. The MDI of MK-4 at age 18-64 years and 65-90 years was 12.8 and 10.2µg/d, respectively.

Intakes of MK-4 were similar between teenagers aged 13-17 years and adults aged 18-64 years and were higher than intakes in pre-school children aged 1-4 years, children aged 5-12 years and older adults aged 65-90 years. At ages 13-17 and 18-64 years, males had significantly higher intakes than females.

Energy adjusted MK-4 intakes were similar between all age groups however, pre-school children had higher intakes than adults aged 65-90 years. MK-4 intakes were similar between males and females of all ages with the exception of males aged 18-64 years having higher intakes than females due to males consuming a more MK-4 nutrient dense diet.

Key sources of MK-4

Table 5 presents the contribution of food groups to the mean daily intake of MK-4 in the Irish population aged 1-90 years. 'Meat & meat products' contributed 50-67% of the MDI of MK-4 (1-4 year olds: 50%, 5-12 year olds: 59%, 13-17 year olds: 66%, 18-64 year olds: 67%, 65-90 year olds: 58%). Of this, 'meat products' (sausages, burgers and meat pies) accounted for 27% of intakes at age 1-4 years, 35% at age 5-12 years, 32% at age 13-17 years, 25% at age 18-64 years and 17% at age 65-90 years. The contribution from 'milk' to the MDI of MK-4 in the Irish population ranged from 8-25% (1-4 year olds: 25%, 5-12 year olds: 22%, 13-17 year olds: 15%, 18-64 year olds: 8%, 65-90 year olds: 10%). The contribution from 'eggs & egg dishes' to intakes of MK-4 ranged from 4-11% across age groups.

The mean daily intake of MK-5-10

Tables 6 and 7 report the mean daily intake of MK-5-10 (µg & µg/10MJ) in the Irish population aged 1 to 90 years split by gender and age group. The MDI of MK-5-10 in pre-school children aged 1-4 years and children aged 5-12 years was 32.4 and 41.7µg/d, respectively. The MDI of MK-5-10 was 43.1µg/d in Irish teenagers aged 13-17 years. The MDI of MK-5-10 in adults aged 18-64 years and 65-90 years was 45.3 and 32.1µg/d, respectively.

Intakes of MK-5-10 were similar between children aged 5-12 years, teenagers aged 13-17 years, adults aged 18-64 years and were higher than intakes in pre-school children aged 1-4 years and older adults aged 65-90 years. At age 18-64 years, males had significantly higher intakes than females.

Energy adjusted intakes of MK-5-10 were similar in pre-school children, children 5-12 years, teenagers 13-17 years and adults 18-64 years and were higher than intakes in adults aged adults aged 65-90 years. MK-5-10 intakes were similar between males and females of all ages with the exception of males aged 18-64 years having higher intakes than females due to males consuming a more MK-5-10 nutrient dense diet.

Key sources of MK-5-10

Table 8 presents the contribution of food groups to the mean daily intake of MK-5-10 in the Irish population aged 1-90 years. ‘Meat & meat products’ was the key source of MK-5-10 (1-4 year olds: 45%, 5-12 year olds: 61%, 13-17 year olds: 56%, 18-64 year olds: 44%, 65-90 year olds: 45%). Of this, ‘sausages’ accounted for 38% of intakes at age 1-4 years, 51% at age 5-12 years, 44% at age 13-17 years, 32% at age 18-64 years and 27% at age 65-90 years. ‘Cheese’ contributed 21-37% of the MDI of MK-5-10 (1-4 year olds: 35%, 5-12 year olds: 21%, 13-17 year olds: 26%, 18-64 year olds: 37%, 65-90 year olds: 34%).

Table 1. The mean daily intake of total MK (MK-4-10) (μg/d) in the Irish population aged 1-90 years

	MK-4-10 (μg/d)												
	All				**Males**				**Females**				**P-value**
Age (years)	**Mean**	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**	
1-4 years (*n* 500)	40.1[a]	42.4	22.9	10.7-56.2	40.9	43.1	22.2	10.3-58.8	39.3	41.6	23.3	10.8-55.2	**0.925**
1 y (n 126)	*33.0*	*42.0*	*15.3*	*8.3-43.7*	*27.1*	*33.7*	*13.8*	*6.9-33.1*	*38.9*	*48.6*	*21.3*	*10.7-52.9*	
2-4 y (n 374)	*42.5*	*42.3*	*24.8*	*10.7-62.6*	*45.5*	*45.0*	*26.1*	*10.7-69.4*	*39.4*	*39.2*	*23.8*	*10.9-55.6*	
5-12 years (*n* 594)	51.8[b]	46.9	38.9	17.3-71.1	55.3	50.0	44.4	17.4-72.3	48.3	43.7	34.0	17.1-66.6	**0.085**
5-8 y (n 296)	*53.6*	*43.5*	*43.9*	*18.6-72.0*	*55.6*	*42.9*	*49.7*	*17.8-74.3*	*51.8*	*44.2*	*39.0*	*18.8-66.6*	
9-12 y (n 298)	*49.9*	*50.1*	*32.6*	*16.1-68.4*	*55.1*	*56.2*	*38.6*	*16.5-69.8*	*44.8*	*43.0*	*29.8*	*15.0-66.6*	
13-17 years (*n* 441)	55.3[b]	49.5	40.2	20.7-73.2	66.1	57.8	49.7	22.9-88.4	44.1*	36.2	33.1	17.8-61.2	**0.000**
13-14 y (n 188)	*57.5*	*50.5*	*41.6*	*20.8-82.3*	*71.3*	*60.4*	*54.1*	*22.6-101*	*43.3*	*32.7*	*33.1*	*19.5-61.2*	
15-17 y (n 253)	*53.7*	*48.8*	*40.1*	*20.6-70.8*	*62.3*	*55.7*	*48.5*	*24.4-75.0*	*44.8*	*38.7*	*33.4*	*16.9-60.8*	
18-64 years (*n* 1274)	58.1[b]	67.7	31.5	15.8-75.6	74.0	78.1	42.7	21.1-104	42.4*	50.8	23.7	12.8-51.8	**0.000**
65-90 years (*n* 226)	42.3[a]	52.5	19.5	9.1-56.4	54.9	63.8	26.6	10.1-75.3	31.1	36.7	16.1	8.3-35.4	**0.012**

Differences between gender were assessed using Mann-Whitney U tests with significant differences ($P<0.001$) denoted by *
Differences between age groups were assed using a Kruscal Wallis test ($P=0.000$) with differences denoted by different superscript lower case letters
MK-4-10 intakes were similar among children aged 5-12 y and 13-17 y ($P=0.115$) and adults 18-64 y ($P=0.355$); intakes in pre-school children 1-4 y and older adults 65-90 y had significantly lower intakes than all other age groups ($P=0.000$)

Table 2. The mean daily intake of total MK (MK-4-10) (μg/10MJ) in the Irish population aged 1-90 years

	MK-4-10 (μg/10MJ)												P-value
	All				**Males**				**Females**				
Age (years)	**Mean**	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**	
1-4 years (*n* 500)	84.5[a,b]	88.1	45.5	22.8-124	83.5	88.8	42.5	21.6-129	85.6	87.6	46.4	23.2-123	**0.462**
1 y (n 126)	*75.9*	*89.0*	*39.9*	*21.4-105*	*64.3*	*81.4*	*32.0*	*18.1-73.9*	*87.5*	*95.2*	*46.1*	*25.5-122*	
2-4 y (n 374)	*87.5*	*87.7*	*50.5*	*23.0-131*	*89.9*	*90.4*	*52.1*	*22.7-138*	*85.0*	*85.1*	*47.0*	*23.1-124*	
5-12 years (*n* 594)	75.2[a]	67.3	58.6	23.4-101	76.1	67.1	63.8	22.5-103	74.4	67.6	52.2	23.8-99.0	**0.651**
5-8 y (n 296)	*81.9*	*64.3*	*68.0*	*30.6-111*	*80.9*	*57.6*	*71.5*	*28.8-113*	*82.9*	*70.2*	*63.7*	*31.6-104.2*	
9-12 y (n 298)	*68.6*	*69.6*	*45.9*	*20.6-89.1*	*71.4*	*75.2*	*48.7*	*20.0-87.4*	*65.9*	*63.9*	*45.1*	*21.2-89.5*	
13-17 years (*n* 441)	66.6[a,b]	54.4	51.4	24.9-91.7	71.2	60.9	52.4	24.7-103	61.8	46.5	50.4	25.0-82.1	**0.366**
13-14 y (n 188)	*71.3*	*59.0*	*56.4*	*26.3-96.8*	*80.9*	*70.4*	*60.4*	*29.2-118*	*61.5*	*42.7*	*54.6*	*25.4-82.8*	
15-17 y (n 253)	*63.1*	*50.6*	*48.7*	*24.3-80.2*	*64.0*	*52.0*	*48.9*	*23.1-77.4*	*62.1*	*49.3*	*47.6*	*24.6-81.9*	
18-64 years (*n* 1274)	66.0[b]	72.6	36.7	20.6-85.7	74.1	77.0	45.1	21.9-101	58.0*	67.0	33.5	18.8-72.2	**0.000**
65-90 years (*n* 226)	58.1[c]	74.9	26.8	13.9-74.1	66.6	79.2	35.1	13.8-83.0	50.5	70.3	23.9	14.0-52.0	**0.224**

Differences between gender were assessed using Mann-Whitney U tests with significant differences (P<0.001) denoted by *
Differences between age groups were assed using a Kruscal Wallis test (P=0.000) with differences denoted by different superscript lower case letters
MK-4-10 intakes in pre-school children 1-4 y were similar to intakes in children 5-12 y (P=0.878), teenagers 13-17 y (P=0.674) and adults 18-64 y (P=0.001); pre-school children 1-4 y had higher intakes than older adults aged 65-90 years (P=0.000)

Table 3. The mean daily intake of MK-4 (μg/d) in the Irish population aged 1-90 years

	MK-4 (μg/d)												**P-value**
	All				**Males**				**Females**				
Age (years)	**Mean**	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**	
1-4 years (*n* 500)	7.7[a]	4.0	7.0	4.7-9.9	7.8	4.1	7.1	4.8-9.9	7.6	3.9	6.9	4.7-9.6	**0.593**
1 y (n 126)	*7.0*	*4.2*	*6.5*	*3.9-8.9*	*6.4*	*3.1*	*6.3*	*4.1-7.8*	*7.6*	*5.1*	*6.6*	*3.7-9.8*	
2-4 y (n 374)	*8.0*	*3.9*	*7.1*	*5.0-10.2*	*8.3*	*4.3*	*7.4*	*5.0-10.7*	*7.6*	*3.5*	*7.1*	*4.9-9.6*	
5-12 years (*n* 594)	10.1[b]	4.4	9.5	6.8-12.2	10.7	4.7	10.4	7.4-13.1	9.5*	4.1	8.3	6.5-11.8	**0.000**
5-8 y (n 296)	*10.0*	*4.2*	*9.2*	*6.8-12.1*	*10.3*	*4.1*	*10.2*	*7.3-12.4*	*9.7*	*8.3*	*4.2*	*6.6-12.0*	
9-12 y (n 298)	*10.2*	*4.7*	*9.6*	*6.8-12.4*	*11.1*	*5.1*	*10.7*	*7.5-13.6*	*9.3*	*4.1*	*8.3*	*6.3-11.7*	
13-17 years (*n* 441)	12.3[c]	5.9	11.3	8.6-15.4	14.6	6.1	13.5	10.7-17.7	10.0*	4.5	9.5	6.7-12.3	**0.000**
13-14 y (n 188)	*12.3*	*6.0*	*10.9*	*8.1-15.5*	*14.8*	*6.4*	*13.0*	*10.3-18.2*	*9.8*	*4.3*	*9.5*	*6.3-12.0*	
15-17 y (n 253)	*12.4*	*5.8*	*11.6*	*8.7-15.2*	*14.5*	*5.9*	*13.8*	*10.8-17.4*	*10.2*	*4.7*	*9.5*	*6.9-12.4*	
18-64 years (*n* 1274)	12.8[c]	7.4	11.3	7.5-16.4	15.6	8.0	14.2	9.9-19.7	10.0*	5.5	9.2	6.1-12.8	**0.000**
65-90 years (*n* 226)	10.2[b]	6.8	8.7	5.6-12.8	11.4	7.8	9.5	5.8-14.2	9.1	5.5	8.2	5.4-11.8	**0.062**

Differences between gender were assessed using Mann-Whitney U tests with significant differences ($P<0.001$) denoted by *
Differences between age groups were assed using a Kruscal Wallis test ($P=0.000$) with differences denoted by different superscript lower case letters
MK-4 intakes were similar between teenagers 13-17 y and adults 18-64 y ($P=0.885$) and were higher than intakes in pre-school children 1-4 y ($P=0.000$), children 5-12 y ($P=0.000$) and older adults 65-90 y ($P=0.000$)

Table 4. The mean daily intake of MK-4 (µg/10MJ) in the Irish population aged 1-90 years

	MK-4 (µg/10MJ)												
	All				**Males**				**Females**				**P-value**
Age (years)	**Mean**	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**	
1-4 years (*n* 500)	16.2[a]	7.7	14.5	10.6-20.9	16.0	7.7	14.2	10.5-20.3	16.4	7.7	14.6	10.9-21.4	**0.517**
1 y (n 126)	*16.3*	*8.6*	*14.7*	*10.5-21.5*	*15.3*	*7.2*	*13.9*	*10.6-18.3*	*17.3*	*9.7*	*15.9*	*9.4-23.6*	
2-4 y (n 374)	*16.2*	*7.5*	*14.3*	*10.7-20.7*	*16.3*	*7.9*	*14.4*	*10.4-21.1*	*16.1*	*7.0*	*14.2*	*11.0-20.1*	
5-12 years (*n* 594)	14.5[a,c]	6.0	13.4	10.4-17.7	14.6	5.8	14.1	10.7-18.0	14.4	6.2	13.0	10.2-17.4	**0.254**
5-8 y (n 296)	*15.2*	*5.7*	*14.3*	*11.2-18.3*	*15.2*	*5.0*	*14.5*	*11.9-18.3*	*15.3*	*6.3*	*13.6*	*10.8-18.5*	
9-12 y (n 298)	*13.8*	*6.2*	*12.8*	*9.8-16.6*	*14.1*	*6.5*	*13.3*	*10.2-17.2*	*13.6*	*5.9*	*12.0*	*9.4-15.9*	
13-17 years (*n* 441)	14.8[a,b]	5.6	14.4	11.0-17.8	15.6	5.8	15.4	11.6-18.2	14.0	5.2	13.5	10.5-17.2	**0.003**
13-14 y (n 188)	*15.2*	*5.9*	*14.6*	*10.8-18.0*	*16.5*	*6.3*	*15.7*	*12.1-18.8*	*13.8*	*5.2*	*13.1*	*10.4-16.8*	
15-17 y (n 253)	*14.6*	*5.2*	*14.3*	*11.0-17.3*	*15.0*	*5.3*	*14.8*	*11.5-17.7*	*14.2*	*5.2*	*13.7*	*10.9-17.2*	
18-64 years (*n* 1274)	15.0[a,c]	7.5	13.5	9.9-18.5	15.9	7.7	14.6	10.7-19.5	14.1*	7.3	12.7	9.2-17.6	**0.000**
65-90 years (*n* 226)	14.1[b,c]	8.6	12.5	8.4-17.4	14.2	9.2	12.1	7.7-17.3	14.0	8.1	12.7	8.7-17.5	**0.582**

Differences between gender were assessed using Mann-Whitney U tests with significant differences (P<0.001) denoted by *
Differences between age groups were assed using a Kruscal Wallis test (P=0.000) with differences denoted by different superscript lower case letters
MK-4 intakes were similar between pre-school children 1-4 y and children 5-12 y (0.002), teenagers 13-17 y (0.116) and adults 18-64 y (P=0.001); intakes in pre-school children were significantly higher than intakes in adults 65-90 y (P=0.000)

Table 5. Contribution (µg & %) of food groups to the mean daily intake of MK-4 in the Irish population aged 1-90 years

	1-4 year olds (*n* 500)		**5-12 year olds (*n* 594)**		**13-17 year olds (*n* 441)**		**18-64 years (*n* 1274)**		**65-90 years (*n* 226)**	
Food groups	**µg**	**%**	**µg**	**%**	**µg**	**%**	**µg**	**%**	**µg**	**%**
Meat & meat products	**4.2**	**50.0**	**6.3**	**59.0**	**8.4**	**66.3**	**9.1**	**66.6**	**6.2**	**58.3**
Meat products (sausages, burgers, meat pies)	*2.6*	*26.8*	*4.0*	*35.3*	*4.2*	*31.7*	*4.0*	*25.2*	*2.4*	*16.8*
Fresh meat & poultry	*0.9*	*11.8*	*1.4*	*14.1*	*2.8*	*22.4*	*3.4*	*28.2*	*3.0*	*31.7*
Meat dishes	*0.7*	*11.5*	*0.9*	*9.5*	*1.4*	*12.3*	*1.7*	*13.3*	*0.8*	*9.8*
Milk	**1.8**	**24.6**	**2.0**	**21.9**	**1.8**	**14.5**	**1.0**	**8.2**	**0.9**	**10.2**
Eggs & egg dishes	**0.5**	**6.2**	**0.5**	**4.7**	**0.5**	**4.2**	**1.0**	**8.2**	**1.0**	**10.7**
Yogurt & fromage frais	0.4	5.9	0.2	2.6	0.1	1.2	0.1	1.4	0.2	2.5
Cheese	0.4	5.4	0.3	3.6	0.5	4.7	0.6	5.7	0.5	5.4
Butter, spreading fats & oils	0.2	2.7	0.3	2.5	0.4	2.9	0.5	4.1	0.8	5.2
Creams, ice-creams & chilled desserts	0.1	1.9	0.2	2.2	0.2	1.9	0.2	1.9	0.3	3.0
Potatoes & potato products	0.1	1.4	0.1	0.9	0.2	1.4	0.1	1.2	0.2	1.6
Sugars, confectionery, preserves & savoury snacks	0.1	0.9	0.2	1.9	0.2	1.8	0.1	1.0	0.0	0.4
Fish & fish dishes	0.0	0.5	0.0	0.2	0.0	0.2	0.1	0.8	0.1	2.0
Grains, rice, pasta & savouries	0.0	0.2	0.0	0.6	0.1	0.7	0.1	0.5	0.0	0.1
Vegetable & vegetable dishes	0.0	0.2	0.0	0.1	0.0	0.3	0.0	0.3	0.0	0.5
Bread & rolls	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Breakfast cereals	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Biscuits, cakes & pastries	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Fruit & fruit juices	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Beverages	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Soups, sauces & miscellaneous foods	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Nuts, seeds, herbs & spices	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total	**7.7**	**100**	**10.1**	**100**	**12.3**	**100**	**12.8**	**100**	**10.2**	**100**

Table 6. The mean daily intake of MK-5-10 (μg/d) in the Irish population aged 1-90 years

	MK-5-10 (μg/d)												P-value
	All				**Males**				**Females**				
Age (years)	**Mean**	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**	
1-4 years (*n* 500)	32.4[a,c]	39.1	15.6	4.5-48.5	33.0	39.9	15.6	3.9-50.5	31.7	38.5	15.6	5.3-46.0	0.751
1 y (n 126)	*26.0*	*38.5*	*9.5*	*3.8-37.1*	*20.7*	*31.5*	*7.9*	*1.9-26.2*	*31.4*	*44.1*	*13.6*	*5.8-43.1*	
2-4 y (n 374)	*34.5*	*39.2*	*18.6*	*4.7-52.4*	*37.2*	*41.6*	*20.1*	*4.6-59.7*	*31.9*	*36.5*	*16.6*	*4.7-48.3*	
5-12 years (*n* 594)	41.7[b]	43.4	29.8	8.7-59.4	44.7	46.3	34.7	7.9-62.0	38.9	40.3	25.0	9.4-54.3	0.191
5-8 y (n 296)	*43.7*	*40.1*	*34.6*	*11.7-62.0*	*45.3*	*39.5*	*38.4*	*9.5-64.6*	*42.2*	*40.7*	*30.6*	*11.7-57.0*	
9-12 y (n 298)	*39.8*	*46.4*	*23.7*	*7.8-56.0*	*44.1*	*52.1*	*29.6*	*6.9-56.6*	*35.6*	*39.7*	*22.2*	*8.2-53.4*	
13-17 years (*n* 441)	43.1[b]	45.4	29.8	9.8-60.4	51.6	53.4	36.6	9.7-74.1	34.3	33.0	25.4	9.8-49.6	0.004
13-14 y (n 188)	*45.3*	*45.9*	*30.0*	*10.7-67.7*	*56.5*	*55.6*	*40.2*	*9.8-86.3*	*33.7*	*29.4*	*25.6*	*10.9-51.5*	
15-17 y (n 253)	*41.4*	*45.0*	*29.8*	*9.3-57.8*	*47.9*	*51.7*	*35.0*	*9.7-60.4*	*34.7*	*35.6*	*25.0*	*9.0-48.8*	
18-64 years (*n* 1274)	45.3[a,b]	61.8	21.4	6.1-59.5	58.3	71.8	29.5	8.4-86.0	32.4*	46.6	14.5	5.0-42.5	0.000
65-90 years (*n* 226)	32.1[c]	47.2	10.7	1.6-43.9	43.5	57.4	17.3	2.5-63.5	22.0	33.0	9.1	1.2-24.0	0.003

Differences between gender were assessed using Mann-Whitney U tests with significant differences (P<0.001) denoted by *
Differences between age groups were assessed using a Kruskal Wallis test (P=0.000) with differences denoted by different superscript lowercase letters
MK-5-10 intakes were similar between children 5-12 y and teenagers 13-17 y (P=0.624), adults 18-64 y (P=0.012) and were higher than intakes in pre-school children 1-4 y (P=0.000) and older adults 65-90 y (P=0.000)

Table 7. The mean daily intake of MK-5-10 (µg/10MJ) in the Irish population aged 1-90 years

	MK-5-10 (µg/10MJ)												
	All				**Males**				**Females**				
Age (years)	**Mean**	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**	**P-value**
1-4 years (*n* 500)	68.3[a,c]	81.8	31.8	10.4-104	67.5	82.5	30.8	8.0-106	69.2	81.3	32.4	11.6-101	**0.415**
1 y (n 126)	*59.6*	*82.0*	*24.6*	*9.0-89.6*	*49.0*	*75.9*	*19.6*	*4.2-56.4*	*70.2*	*86.9*	*34.2*	*14.0-101*	
2-4 y (n 374)	*71.3*	*81.6*	*37.0*	*10.8-111*	*73.7*	*83.8*	*40.3*	*9.1-116*	*68.8*	*79.5*	*32.3*	*11.0-102*	
5-12 years (*n* 594)	60.8[a]	62.3	44.9	13.3-85.2	61.6	62.3	49.8	12.1-87.2	60.1	62.3	39.1	14.7-81.3	**0.763**
5-8 y (n 296)	*66.8*	*59.5*	*53.7*	*18.9-93.8*	*65.9*	*53.7*	*57.4*	*16.5-98.5*	*67.7*	*64.8*	*49.7*	*18.9-87.4*	
9-12 y (n 298)	*54.9*	*64.4*	*32.8*	*9.8-73.1*	*57.4*	*69.6*	*35.4*	*8.7-70.3*	*52.5*	*59.0*	*30.9*	*10.6-77.5*	
13-17 years (*n* 441)	51.9[a]	50.6	37.5	13.2-74.7	55.6	56.7	37.5	10.9-87.1	48.0	43.1	38.2	14.8-66.1	**0.657**
13-14 y (n 188)	*56.3*	*54.4*	*42.5*	*15.4-79.6*	*64.5*	*65.3*	*47.0*	*13.9-95.1*	*47.9*	*38.8*	*41.6*	*16.0-66.6*	
15-17 y (n 253)	*48.6*	*47.4*	*35.1*	*10.6-63.6*	*49.1*	*48.7*	*33.3*	*9.9-62.5*	*48.1*	*46.3*	*35.5*	*12.5-65.8*	
18-64 years (*n* 1274)	51.0[b,c]	67.1	25.0	8.1-70.8	58.3	71.3	30.2	9.5-82.2	43.9*	62.0	19.9	7.2-57.0	**0.000**
65-90 years (*n* 226)	44.0[b]	68.0	15.9	2.7-62.3	52.5	71.5	22.6	4.0-71.6	36.5	64.0	12.9	2.1-34.0	**0.030**

Differences between gender were assessed using Mann-Whitney U tests with significant differences (P<0.001) denoted by *
Differences between age groups were assessed using a Kruskal Wallis test (P=0.000) with differences denoted by different superscript lowercase letters
MK-5-10 intakes were similar in pre-school children 1-4 y and children 5-12 y (P=0.419), teenagers 13-17 y (P=0.754) and were higher than intakes in adults aged adults aged 65-90 years (P=0.000)

Table 8. Contribution (μg & %) of food groups to the mean daily intake of MK-5-10 in the Irish population aged 1-90 years

	1-4 year olds (*n* 500)		**5-12 year olds (*n* 594)**		**13-17 year olds (*n* 441)**		**18-64 years (*n* 1274)**		**65-90 years (*n* 226)**	
Food groups	**μg**	**%**	**μg**	**%**	**μg**	**%**	**μg**	**%**	**μg**	**%**
Meat & meat products	**26.1**	**44.5**	**35.3**	**61.2**	**33.3**	**56.0**	**34.2**	**43.9**	**24.2**	**44.5**
Sausages	*25.2*	*38.1*	*33.0*	*51.1*	*29.6*	*43.6*	*32.0*	*31.5*	*22.5*	*26.5*
Fresh meat & poultry	*0.1*	*3.2*	*0.2*	*2.8*	*0.3*	*4.0*	*0.5*	*7.0*	*0.5*	*15.5*
Meat dishes	*0.2*	*1.2*	*0.7*	*1.8*	*0.5*	*1.8*	*0.4*	*2.1*	*0.3*	*0.7*
Meat products (burgers, meat pies)	*0.7*	*1.9*	*1.4*	*5.6*	*2.9*	*6.7*	*1.3*	*3.4*	*0.9*	*1.8*
Cheese	**5.3**	**34.7**	**4.8**	**20.9**	**7.5**	**26.1**	**9.2**	**37.2**	**7.1**	**33.8**
Milk & yogurt	**0.4**	**14.1**	**0.4**	**6.8**	**0.3**	**4.5**	**0.2**	**5.6**	**0.2**	**8.7**
Fish & fish dishes	0.1	2.4	0.1	0.8	0.1	1.1	0.1	3.1	0.2	5.8
Grains, rice, pasta & savouries	0.3	2.2	1.1	8.9	1.7	11.1	1.2	6.4	0.1	1.5
Vegetable & vegetable dishes	0.1	0.9	0.0	0.2	0.0	0.1	0.1	1.2	0.2	1.6
Eggs & egg dishes	0.1	0.5	0.1	0.5	0.1	0.2	0.1	0.8	0.1	0.3
Creams, ice-creams & chilled desserts	0.0	0.4	0.0	0.4	0.0	0.3	0.0	0.8	0.0	1.9
Bread & rolls	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Breakfast cereals	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Biscuits, cakes & pastries	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Butter, spreading fats & oils	0.0	0.1	0.0	0.2	0.0	0.3	0.0	0.8	0.0	1.4
Potatoes & potato products	0.0	0.1	0.0	0.1	0.0	0.2	0.0	0.3	0.0	0.4
Fruit & fruit juices	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Beverages	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Sugars, confectionery, preserves & savoury snacks	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Soups, sauces & miscellaneous foods	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Nuts, seeds, herbs & spices	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total	**32.4**	**100**	**41.7**	**100**	**43.1**	**100**	**45.3**	**100**	**32.1**	**100**

Discussion

The aim of this study was to estimate the intakes and key dietary sources of menaquinones (menaquinone-4 & menaquinone-5-10) in the Irish population aged 1-90 years using the updated vitamin K composition data as described in chapter 3. Mean intakes of total MK (MK-4-10) ranged from 40-58µg/d across age groups with mean intakes of MK-4 and MK-5-10 ranging from 8-13µg/d and 32-45 µg/d, respectively. Key dietary sources of MK-4 and MK-5-10 in the Irish population were ‘meat & meat products’, ‘milk’ and ‘cheese’.

These findings are discussed in more detail below in context with the available literature and potential health implications. Due to differences in the origin and bioavailability of the individual menaquinones, MK-4 and MK-5-10 are discussed separately.

MK-4

MK-4 is unique amongst the menaquinones as it is not synthesised by bacteria. It is formed in mammals from the tissue specific conversion from phylloquinone or from menadione (a synthetic form of vitamin K, which may be added to animal feed) (Dialameh *et al.*, 1971, Okano *et al.*, 2008, EFSA Panel on Additives and Products or Substances used in Animal Feed, 2014). Mean intakes of MK-4 in children aged 1-17 years ranged from 8-12µg/d across age groups. In adults, aged 18-64 and 65-90 years, mean intakes of MK-4 were 12.8 and 10.2µg/d, respectively. While some differences in MK-4 intakes were observed across age groups it was typically due to differences in energy intakes with the exception of pre-school children aged 1-4 years who had a more MK-4 dense diet. There are currently no national dietary surveys across Europe or the US that report the intakes of menaquinones in healthy population groups. Studies investigating menaquinone intakes and their association with specific health outcomes (such as bone health, cardiovascular health and cancer) have reported intakes of MK-4 within the range of 7-14µg/d in adults of all ages. (Schurgers *et al.*, 1999, Geleijnse *et al.*, 2004, Nimptsch *et al.*, 2008, Beulens *et al.*, 2009, Gast *et al.*, 2009, Apalset *et al.*, 2010, Beulens *et al.*, 2010, Nimptsch *et al.*, 2010, Apalset *et al.*, 2011, Vissers *et al.*, 2013). These intakes are similar to intakes reported in this study in Irish adults.

'Meat & meat products' was the key source of MK-4 in the Irish population (50-67%, range across age groups). The contribution from 'meat & meat products' to intakes of MK-4 was 50% at age 1-4 years, 59% at age 5-12 years, 66% at age 13-17 years, 67% at age 18-64 years and 58% at age 65-90 years. The increasing contribution from meat from childhood through to adulthood and lower contribution from meat in older adults may be explained by the increase in consumption of meat with age group up to adulthood followed by a decrease in older adults (1-4 year olds: 80g/d, 5-12 year olds: 104g/d, 13-17 year olds: 160g/d, 18-64 year olds: 183g/d, 65-90 year olds: 154g/d) (www.iuna.net). Milk was a key source of MK-4 in pre-school children aged 1-4 years and children aged 5-12 years with a decrease in contribution in teenagers, adults and older adults reflecting the pattern of milk consumption across the life cycle (1-4 year olds: 313g, 5-12 year olds: 276g, 13-17 year olds: 257g, 18-64 year olds: 212g, 65-90 year olds: 196g) (www.iuna.net). To the best of this authors' knowledge, this study is the first to report the sources of MK-4 in adults and children using data collected during national dietary surveys and therefore it is difficult to compare our results to that of others.

MK-5-10

The longer chained menaquinones (MK-5-10) are exclusively synthesized by bacteria. There are differences in the concentration and forms of menaquinones produced in a food depending on the bacteria used in the fermentation process (Manoury *et al.*, 2013). Mean intakes of MK-5-10 in children aged 1-17 years ranged from 32-43µg/d across age groups. Intakes of MK-5-10 in adults aged 18-64 and 65-90 years were 45.3 and 32.1µg/d, respectively. While there were some difference in MK-5-10 intakes across age groups, when intakes were adjusted for energy, pre-school children aged 1-4 years had higher intakes than teenagers and adults adding to the body of evidence that young children in Ireland have a relatively micronutrient-dense diet (Browne *et al.*, 2012, Hennessy *et al.*, 2012, Walton *et al.*, 2017).

Studies examining menaquinone intakes and their association with specific health outcomes in adult population groups have reported MK-5-10 intakes generally within the range of 18-22µg/d (Schurgers *et al.*, 1999, Geleijnse *et al.*, 2004, Nimptsch *et al.*, 2008, Beulens *et al.*, 2009, Gast *et al.*, 2009, Apalset *et al.*, 2010, Beulens *et al.*, 2010, Nimptsch *et al.*, 2010, Apalset *et al.*, 2011, Vissers *et al.*, 2013, Zwakenberg *et al.*, 2017). These intakes are lower than intakes in Irish adults, which may be partly explained by the detailed brand and recipe level data used in the current study to estimate menaquinone intakes. Further research is needed to estimate the intakes of menaquinones in national dietary surveys across Europe to allow direct comparison to intakes in the Irish population.

'Meat & meat products' was the key source of MK-5-10 in the Irish population (44-61% range across age groups). Of the 'meat & meat products', 'sausages' accounted for between 27-51% of MK-5-10 intakes in the Irish population (1-4 year olds; 38%, 5-12 year olds; 51%, 13-17 year olds; 44%, 18-64 year olds; 32%, 65-90 year olds; 27%). Analytical data from a recent study in the U.S was the first to report high concentrations of some menaquinone forms in pork products, including sausages (Fu *et al.*, 2016). Although the origin of these menaquinone forms is not yet fully understood, it has been suggested they may be absorbed from the intestine where menaquinones are produced by gut bacteria (Walther *et al.*, 2013). Cheese has been identified as an important source of menaquinones in the Western diet with variations in the types and concentration of menaquinones present depending on the bacterial starter culture used (Schurgers and Vermeer, 2000, Vermeer *et al.*, 2018). In the current study, the contribution from 'cheese' to MK-5-10 intakes ranged from 21-37% across age groups. There are few data available on the sources of MK-5-10 in adults or children however; two studies in adults investigating menaquinone intake and their association with specific health outcomes reported that dairy products (60%), especially cheese (43-53%), and meat and meat products (17%) were key contributors to intakes of the menaquinones (Nimptsch *et al.*, 2008, Beulens *et al.*, 2010).

Public Health Implications

There is growing evidence suggesting that the menaquinones may have an important role in the acquisition of bone mass and a recent study has reported a positive association between some menaquinones and cognition in older adults (Van Summeren *et al.*, 2009, Knapen *et al.*, 2013, McCann *et al.*, 2019). Furthermore, some studies have suggested that the menaquinones may reduce the risk of certain chronic diseases including coronary heart disease and type-2 diabetes (Beulens *et al.*, 2009, Gast *et al.*, 2009, Beulens *et al.*, 2010). Menaquinones have been shown to be more bioavailable than vitamin K_1. As little as 10-15% of vitamin K_1 in green vegetables is absorbed in the body compared to menaquinone bioavailability which is thought to be far higher with almost complete absorption from dairy products (Gijsbers *et al.*, 1996, Schurgers and Vermeer, 2000). Differences also exist in the bioavailability of individual menaquinones. MK-7 has been shown to increase serum levels significantly in comparison to MK-4 when consumed at a nutritional level dose (Sato *et al.*, 2012). This may be explained when we consider that the longer chained menaquinones (including MK-7) have a very long half-life in comparison to that of vitamin K_1 or MK-4 allowing additional time for extrahepatic functions such as the carboxylation of osteocalcin (Schurgers and Vermeer, 2000, Schurgers and Vermeer, 2002, Schurgers *et al.*, 2007). The contribution of menaquinones to vitamin K nutrition may currently be underestimated and warrants further investigation.

Strengths and limitations

The main strengths of the present study include the use of nationally representative dietary data to conduct our analysis. Detailed dietary intake data were collected at brand level supported by the food packaging collected during the survey and recipes of composite dishes. While there was limited analytical data available for Irish and UK foods, this study used the most appropriate methodology to apply composition values to the IFCD (2012) (chapter 3), which included the calculation of menaquinone composition of recipes at ingredient level. This allowed for the most accurate assessment of menaquinone intakes in the Irish population.

Conclusions

This study is the first to report the intakes and sources of menaquinones in nationally representative samples of the Irish population. Mean intakes of total MK (MK-4-10) ranged from 40-58µg/d across age groups with mean intakes of MK-4 and MK-5-10 ranging from 8-13µg/d and 32-45 µg/d, respectively. ‘Meat & meat products’ was the key source of both MK-4 and MK-5-10 across all age and gender population groups examined. ‘Cheese’ and ‘milk’ are also important contributors to intakes of menaquinones in the Irish diet. These findings highlight the contribution of staple foods to vitamin K_2 intakes in the Irish diet. Further research is required to establish the role of menaquinones in human health and the bioavailability of both short and long chain menaquinone forms. This study will be important for the food industry and other researchers investigating the intakes and key dietary sources of menaquinones in other population groups.

References

Apalset, E., Gjesdal, C. G., Eide, G. E. & Tell, G. S. (2011). Intake of vitamin K1 and K2 and risk of hip fractures: The Hordaland Health Study. *Bone,* 49**,** 990-5.

Apalset, E. M., Gjesdal, C. G., Eide, G. E., Johansen, A.-M. W., Drevon, C. A. & Tell, G. S. (2010). Dietary vitamins K1, K2 and bone mineral density: the Hordaland Health Study. *Archives of Osteoporosis,* 5**,** 73-81.

Beulens, J. W., Bots, M. L., Atsma, F., Bartelink, M. L., Prokop, M., Geleijnse, J. M., Witteman, J. C., Grobbee, D. E. & van der Schouw, Y. T. (2009). High dietary menaquinone intake is associated with reduced coronary calcification. *Atherosclerosis,* 203**,** 489-93.

Beulens, J. W., van der, A. D., Grobbee, D. E., Sluijs, I., Spijkerman, A. M. & van der Schouw, Y. T. (2010). Dietary phylloquinone and menaquinones intakes and risk of type 2 diabetes. *Diabetes Care,* 33**,** 1699-705.

Browne, F., Walton, J., McNulty, B., Nugent, A., Gibney, M. & Flynn, A. (2012). Mineral intakes in Irish pre-school children aged 1–4 years. *Proceedings of the Nutrition Society,* 71**,** E96.

Conly, J. M., Stein, K., Worobetz, L. & Rutledge-Harding, S. (1994). The contribution of vitamin K2 (menaquinones) produced by the intestinal microflora to human nutritional requirements for vitamin K. *American Journal of Gastroenterology,* 89**,** 915-23.

Dialameh, G. H., Taggart, W. V., Matschiner, J. T. & Olson, R. E. (1971). Isolation and characterization of menaquinone-4 as a product of menadione metabolism in chicks and rats. *International Journal for Vitamin and Nutrition Research,* 41**,** 391-400.

EFSA Panel on Additives and Products or Substances used in Animal Feed (2014). Scientific Opinion on the safety and efficacy of vitamin K3 (menadione sodium bisulphite and menadione nicotinamide bisulphite) as a feed additive for all animal species. *EFSA Journal,* 12**,** 3532.

EFSA Panel on Dietetic Products, N., Allergies, Turck, D., Bresson, J.-L., Burlingame, B., Dean, T., Fairweather-Tait, S., Heinonen, M., Hirsch-Ernst, K. I., Mangelsdorf, I., McArdle, H. J., Naska, A., Nowicka, G., Pentieva, K., Sanz, Y., Siani, A., Sjödin, A., Stern, M., Tomé, D., Van Loveren, H., Vinceti, M., Willatts, P., Lamberg-Allardt, C., Przyrembel, H., Tetens, I., Dumas, C., Fabiani, L., Ioannidou, S. & Neuhäuser-Berthold, M. (2017). Dietary reference values for vitamin K. *EFSA Journal,* 15**,** e04780.

Elder, S. J., Haytowitz, D. B., Howe, J., Peterson, J. W. & Booth, S. L. (2006). Vitamin K Contents of Meat, Dairy, and Fast Food in the U.S. Diet. *Journal of Agricultural and Food Chemistry,* 54**,** 463-467.

Fagerland, M. W. (2012). t-tests, non-parametric tests, and large studies—a paradox of statistical practice? *BMC Medical Research Methodology,* 12**,** 78.

Ferreira, D. W. (2006). Vitamin K Contents of Grains, Cereals, Fast-Food Breakfasts, and Baked Goods. *Journal of Food Science,* 71**,** S66-S70.

Food Standards Agency (2002). Food Portion Sizes. London: The Stationary Office.

Foster., E., Hawkins A & Adamson A 2010. *Young Person's Food Atlas: Pre-school. London, Food Standards Agency.*

Fu, X., Harshman, S. G., Shen, X., Haytowitz, D. B., Karl, J. P., Wolfe, B. E. & Booth, S. L. (2017). Multiple Vitamin K Forms Exist in Dairy Foods. *Current Developments in Nutrition,* 1**,** e000638-e000638.

Fu, X., Shen, X., Finnan, E. G., Haytowitz, D. B. & Booth, S. L. (2016). Measurement of Multiple Vitamin K Forms in Processed and Fresh-Cut Pork Products in the U.S. Food Supply. *Journal of Agricultural and Food Chemistry,* 64**,** 4531-5.

Gast, G. C., de Roos, N. M., Sluijs, I., Bots, M. L., Beulens, J. W., Geleijnse, J. M., Witteman, J. C., Grobbee, D. E., Peeters, P. H. & van der Schouw, Y. T. (2009). A high menaquinone intake reduces the incidence of coronary heart disease. *Nutrition, Metabolism, and Cardiovascular Diseases,* 19**,** 504-10.

Geleijnse, J. M., Vermeer, C., Grobbee, D. E., Schurgers, L. J., Knapen, M. H., van der Meer, I. M., Hofman, A. & Witteman, J. C. (2004). Dietary intake of menaquinone is associated with a reduced risk of coronary heart disease: the Rotterdam Study. *Journal of Nutrition,* 134**,** 3100-5.

Gijsbers, B. L., Jie, K. S. & Vermeer, C. (1996). Effect of food composition on vitamin K absorption in human volunteers. *British Journal of Nutrition,* 76**,** 223-9.

Hennessy, Á., Walton, J., McNulty, B., Nugent, A., Gibney, M. & Flynn, A. (2012). Vitamin intakes in Irish pre-school children aged 1–4 years. *Proceedings of the Nutrition Society,* 71**,** E37.

Karl, J. P., Meydani, M., Barnett, J. B., Vanegas, S. M., Barger, K., Fu, X., Goldin, B., Kane, A., Rasmussen, H., Vangay, P., Knights, D., Jonnalagadda, S. S., Saltzman, E., Roberts, S. B., Meydani, S. N. & Booth, S. L. (2017). Fecal concentrations of bacterially derived vitamin K forms are associated with gut microbiota composition but not plasma or fecal cytokine concentrations in healthy adults. *American Journal of Clinical Nutrition,* 106**,** 1052-1061.

Knapen, M. H., Drummen, N. E., Smit, E., Vermeer, C. & Theuwissen, E. (2013). Three-year low-dose menaquinone-7 supplementation helps decrease bone loss in healthy postmenopausal women. *Osteoporosis International,* 24**,** 2499-507.

Krebs-Smith, S. M., Kott, P. S. & Guenther, P. M. (1989). Mean proportion and population proportion: two answers to the same question? *Journal of the American Dietetic Association,* 89**,** 671-6.

Lyons, J., Walton, J. & Flynn, A. (2013). Development of an online database of typical food portion sizes in Irish population groups. *Journal of nutritional science,* 2**,** e25-e25.

Manoury, E., Jourdon, K., Boyaval, P. & Fourcassie, P. (2013). Quantitative measurement of vitamin K2 (menaquinones) in various fermented dairy products using a reliable high-performance liquid chromatography method. *Journal of Dairy Science,* 96**,** 1335-46.

McCann, A., Jeffery, I. B., Ouliass, B., Ferland, G., Fu, X., Booth, S. L., Tran, T. T., O'Toole, P. W. & O'Connor, E. M. (2019). Exploratory analysis of covariation of microbiota-derived vitamin K and cognition in older adults. *The American Journal of Clinical Nutrition*.

Nelson., M., Atkinson M & Meyer J (1997). A photographic atlas of food portion sizes. England: Food Standards Agency.

Nimptsch, K., Rohrmann, S., Kaaks, R. & Linseisen, J. (2010). Dietary vitamin K intake in relation to cancer incidence and mortality: results from the Heidelberg cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC-Heidelberg). *American Journal of Clinical Nutrition,* 91**,** 1348-58.

Nimptsch, K., Rohrmann, S. & Linseisen, J. (2008). Dietary intake of vitamin K and risk of prostate cancer in the Heidelberg cohort of the European Prospective

Investigation into Cancer and Nutrition (EPIC-Heidelberg). *American Journal of Clinical Nutrition,* 87**,** 985-92.

Okano, T., Shimomura, Y., Yamane, M., Suhara, Y., Kamao, M., Sugiura, M. & Nakagawa, K. (2008). Conversion of phylloquinone (Vitamin K1) into menaquinone-4 (Vitamin K2) in mice: two possible routes for menaquinone-4 accumulation in cerebra of mice. *Journal of Biological Chemistry,* 283**,** 11270-9.

Public Health England Composition of Foods Integrated Dataset. 2015. *McCance and Widdowson's The Composition of Foods Integrated Dataset 2015* [Online]. Available: https://www.gov.uk/government/publications/composition-of-foods-integrated-dataset-cofid.

Sato, T., Schurgers, L. J. & Uenishi, K. (2012). Comparison of menaquinone-4 and menaquinone-7 bioavailability in healthy women. *Nutrition Journal,* 11**,** 93.

Schurgers, L. J., Geleijnse, J. M., Grobbee, D. E., Pols, H. A. P., Hofman, A., Witteman, J. C. M. & Vermeer, C. (1999). Nutritional Intake of Vitamins K1 (Phylloquinone) and K2 (Menaquinone) in The Netherlands. *Journal of Nutritional & Environmental Medicine,* 9**,** 115-122.

Schurgers, L. J., Teunissen, K. J., Hamulyak, K., Knapen, M. H., Vik, H. & Vermeer, C. (2007). Vitamin K-containing dietary supplements: comparison of synthetic vitamin K1 and natto-derived menaquinone-7. *Blood,* 109**,** 3279-83.

Schurgers, L. J. & Vermeer, C. (2000). Determination of phylloquinone and menaquinones in food. Effect of food matrix on circulating vitamin K concentrations. *Haemostasis,* 30**,** 298-307.

Schurgers, L. J. & Vermeer, C. (2002). Differential lipoprotein transport pathways of K-vitamins in healthy subjects. *Biochimica et Biophysica Acta,* 1570.

Suttie, J. W. (1995). The importance of menaquinones in human nutrition. *Annual Review of Nutrition,* 15**,** 399-417.

Van Summeren, M. J., Braam, L. A., Lilien, M. R., Schurgers, L. J., Kuis, W. & Vermeer, C. (2009). The effect of menaquinone-7 (vitamin K2) supplementation on osteocalcin carboxylation in healthy prepubertal children. *British Journal of Nutrition,* 102.

Vermeer, C., Raes, J., van 't Hoofd, C., Knapen, M. H. J. & Xanthoulea, S. (2018). Menaquinone Content of Cheese. *Nutrients,* 10.

Vissers, L. E., Dalmeijer, G. W., Boer, J. M., Monique Verschuren, W. M., van der Schouw, Y. T. & Beulens, J. W. (2013). Intake of dietary phylloquinone and menaquinones and risk of stroke. *J Am Heart Assoc,* 2**,** e000455.

Walther, B., Karl, J. P., Booth, S. L. & Boyaval, P. (2013). Menaquinones, bacteria, and the food supply: the relevance of dairy and fermented food products to vitamin K requirements. *Advances in Nutrition,* 4**,** 463-73.

Walton, J., Kehoe, L., McNulty, B., Nugent, A. & Flynn, A. (2017). Nutrient intakes and compliance with nutrient recommendations in children aged 1-4 years in Ireland. *Journal of Human Nutrition and Dietetics,* 30.

Zwakenberg, S. R., den Braver, N. R., Engelen, A. I. P., Feskens, E. J. M., Vermeer, C., Boer, J. M. A., Verschuren, W. M. M., van der Schouw, Y. T. & Beulens, J. W. J. (2017). Vitamin K intake and all-cause and cause specific mortality. *Clinical Nutrition*, 36**,** 1294-1300.

Chapter 6

Changes in the intakes and sources of vitamin K_1 and vitamin K_2 in Irish children in the National Children's Food Survey II (2017-18) since the previous National Children's Food Survey (2003-04)

Introduction

Vitamin K_1 and vitamin K_2 intakes have been estimated previously for the Irish population aged 1-90 years (chapter 4 & 5). Since these analyses, new dietary intake data have become available for Irish children aged 5-12 years from the National Children's Food Survey II (NCFS II) (2017-2018) to update the data from the previous National Children's Food Survey (NCFS) (2003-04) for the same age group. Mean vitamin K_1 intake in Irish children aged 5-12 years in the NCFS (2003-04) was 1.3µg/kg/d, which is above the European Food Safety Authority (EFSA) Adequate Intake (AI) of 1µg/kg/d for vitamin K_1 required to maintain normal blood coagulation (EFSA Panel on Dietetic Products *et al.*, 2017). The NCFS data also showed that the mean intake of vitamin K_1 in Irish children (40µg/d) was lower than intakes reported for children in national surveys in Austria (59-75µg/d for children aged 7-12 years) and the United States (63µg/d for children 6-11 years) (Elmadfa *et al.*, 2012, US Department of Agriculture, 2018). 'Vegetable & vegetable dishes' (29%), 'potatoes & potato products' (15%) and 'meat & meat products' (11%) were the key contributors to vitamin K_1 intake in the NCFS.

For vitamin K_2 in the NCFS (2003-04), mean intake of menaquinone-4-10 (MK-4-10) was 52µg/d in Irish children aged 5-12 years, with mean intakes of menaquinone-4 (MK-4) and menaquinone-5-10 (MK-5-10) of 10 and 42µg/d, respectively. Key sources of MK-4 in Irish children were 'meat & meat products' (59%) and 'milk' (22%), with other food groups contributing less than 5% of MK-4 intakes each. Key sources of MK-5-10 in Irish children were 'meat & meat products' (61%) and 'cheese' (21%).

Summary findings from the NCFS II (2017-18) have identified changes in the patterns of consumption of staple foods in Irish children over the past 15 years, some of which may influence vitamin K_1 and vitamin K_2 intake. The intake of 'fresh meat & meat dishes' and discrete fruit was higher and the intake of total milk and 'potatoes & potato products' was lower in the NCFS II than the NCFS (Irish Universities Nutrition Alliance, 2019). The aim of this chapter is to estimate the current intake and sources of vitamin K_1 and vitamin K_2 in Irish school-aged children from the NCFS II (2017-

18) and to identify any changes in vitamin K_1 and vitamin K_2 intake and sources since the previous NCFS (2003-2004).

Methodology

The analysis for this chapter is based on data from the NCFS II, which was a nationally representative cross-sectional study that collected food and beverage consumption data for 600 children aged 5-12 years in the Republic of Ireland between 2017 and 2018. The NCFS II methodology for sampling, participant recruitment, data collection and food quantification is described in detail in chapter 2, with methods specific to this chapter outlined below. Findings from the NCFS II are compared to the previous NCFS (2003-04), which has a similar overall methodology (described in detail in chapter 2). However, a 7-day weighed food diary was used in the NCFS compared to a 4-day weighed food diary in the NCFS II.

Food intake data collection and quantification (NCFS II)

Habitual food and beverage consumption data were estimated using a 4-day weighed food record. A trained researcher visited each participant in their home three times over the recording period including a training visit to demonstrate how to keep the food diary and use the weighing scales, a second visit 24-36 hours into the recording period to review the diary, check for completeness, and clarify details regarding specific food descriptors and quantities, and a final visit one or two days after the recording period to review the remaining recording days and to collect the diary. For all participants, the study period included at least one weekend day. Detailed information relating to the amount, type, brand and cooking method of all foods and beverages (including nutritional supplements) consumed over the recording period was collected from each participant. Details of recipes of composite dishes were also recorded.

A quantification protocol established by the Irish Universities Nutrition Alliance (IUNA) was used for the NCFS II. This protocol is summarised as follows:

1) Weighed (using the digital food scales provided to each participant) (76%)
2) Manufacturer’s information on product labels (11%)
3) Age appropriate photographic food atlas (7%) (Foster *et al.*, 2010),
4) Standard portion weights (3%) (Food Standards Agency, 2002, Lyons *et al.*, 2013)
5) Household measures (1%)

6) Estimates based on the child's previous eating patterns (only used when no other quantification method was appropriate) (2%)

Data entry

Each food and beverage consumed in the NCFS II was assigned a unique food code based on its nutritional profile at brand level. This included recipes of composite dishes, nutritional supplements, fortified foods and generic Irish foods that were commonly consumed. Dietary data were then entered into the data entry system Nutritics© Software using the unique food code. A total of 2046 food codes were included in the NCFS II database.

Body weight

The weight of each participant was measured by the researcher in their own home in duplicate to the nearest 0.1kg. Participants were weighed whilst wearing light clothes, without shoes and after voiding.

Quality control

A number of quality procedures were put in place in an attempt to minimise error and ensure consistency throughout the collection and data entry of food intake. Each fieldworker was primarily responsible for the collection, quantification, coding and data entry of their own participants' food diaries and questionnaires.

Estimation of vitamin K_1 and vitamin K_2 intakes and sources

Each food code (*n* 2046) was assigned a vitamin K_1, MK-4 and MK-5-10 composition value using the same methodology as outlined in detail in chapter 3. The methodology as applied to NCFS II is outlined below:

<u>Vitamin K_1</u>

- *The UK Composition of Foods Integrated Dataset (COFID)* provided composition data for 30% of food codes, of which, 17% were an exact match and 13% were assigned a value of a similar food product (Public Health England Composition of Foods Integrated Dataset, 2015).
- *The United States Department of Agriculture (USDA) National Nutrient Database* provided composition data for 19% of food codes, of which, 14% were an exact match and 5% were assigned a value of a similar food product

(USDA National Nutrient Database for Standard References Release 28, 2015).

- *Published papers* provided composition data for 3% of food codes (Booth *et al.*, 1993, Bolton-Smith *et al.*, 2000, Dismore *et al.*, 2003, Damon *et al.*, 2005, Presse *et al.*, 2015).
- *Recipes.* The vitamin K_1 content of 34% of food codes was calculated from the composition of the individual ingredients. Where details of ingredients were not available (2%) the value of a similar recipe was assigned.
- *Retail products.* The vitamin K_1 content of 3% of food codes were calculated from the composition of the ingredients listed on food packaging.
- *Manufacturers' information* provided the vitamin K_1 composition values for nutritional supplements, which made up 4% of food codes.
- Foods that did not contain any vitamin K_1 were assigned a composition value of 0µg, which made up 4% of food codes.

Menaquinone-4 and menaquinone-5-10

- A composition value of 0µg was assigned to 45% of food codes that did not contain any MK-4 or MK-5-10.
- *Recipes*. The MK-4 and MK-5-10 composition of 34% of food codes was calculated based on their individual ingredients. The MK-4 and MK-5-10 content of a similar recipe was used for 1% of food codes as details of ingredients were not available.
- *Retail products.* The MK-4 and MK-5-10 content of 2% of food codes were calculated based on their ingredients listed on food packaging.
- *Published analytical values* as reported by Schurgers and Vermeer (2000) and Fu *et al.* (2016) provided MK-4 composition values for 7 and 0.4% of food codes, respectively and provided MK-5-10 composition values for 8 and 0.4% of food codes, respectively. For 5% of food codes, the MK-4 and MK-5-10 composition value of a similar product as reported in the literature was assigned.
- *Manufacturers' information* provided the MK-4 and MK-5-10 composition values for nutritional supplements, which made up 4% of food codes.

Statistical analyses

Using descriptive frequencies, the mean, standard deviation (SD), median and IQR of vitamin K_1 and vitamin K_2 intakes were carried out using SPSS© for Windows™ Version 22.0. Differences in the mean daily intake of vitamin K_1 and vitamin K_2 between gender and age groups (5-8 years & 9-12 years) were assessed using independent sample T-tests regardless of normality (due to the large sample size). As sample size increases so does the robustness of t-tests to identify deviations from normality, thus parametric tests are recommended for large samples (Fagerland, 2012). To minimise type 1 errors (as a result of multiple testing), the Bonferoni adjustment was used by dividing the alpha level (0.005) by the number of comparisons. Therefore, intakes were considered to be significantly different from each other if $P<0.01$. All data were not normally distributed. The non-parametric alternative, Kruskal- Wallis test was used to determine significant differences between independent groups. Where significant differences were identified by the Kruskal- Wallis test, the Mann Whitney U test was used to identify where these differences occurred.

To estimate the key dietary sources of vitamin K_1 and vitamin K_2, all food and drinks consumed were allocated to one of nineteen food groups (Appendix I). The percent contribution of each food group to the mean daily intake of vitamin K_1 and vitamin K_2 were calculated by the mean proportion method (Krebs-Smith *et al.*, 1989) and the key contributors to intakes were determined in order of importance for each age group. This method provides information about the sources that are contributing to the nutrient intake 'per person' and is the preferred method when determining important food sources of a nutrient for individuals in the population group as opposed to investigating the sources of a nutrient within the food supply.

Results

The mean daily intake of vitamin K_1 and vitamin K_2 in the NCFS II

Table 1 reports the mean daily intake of vitamin K_1 (µg/d & µg/kg/d) in Irish children aged 5-12 years split by gender and age group in the NCFS II (2017-18). The Mean Daily Intake (MDI) of vitamin K_1 in Irish children aged 5-12 years was 40.3µg/d and there was no difference in the MDI of vitamin K_1 between boys and girls or between age groups.

Expressed as a function of body weight (µg/kg/d), the MDI of vitamin K_1 was 1.4µg/kg/d and was above the AI of 1µg/kg/d in all gender and age groups examined. Vitamin K_1 intakes (µg/kg/d) at age 5-8 years were significantly (P=0.00) higher than that of children aged 9-12 years.

Table 2 reports the mean daily intake of MK-4-10, MK-4 and MK-5-10 in Irish children aged 5-12 years split by gender and age group in the NCFS II (2017-18). The MDI of MK-4-10 was 47.8µg/d, with mean intakes of MK-4 and MK-5-10 of 9.6 and 38.2µg/d, respectively. The MDI of MK-4-10, MK-4 and MK-5-10 were higher in boys than girls however, when adjusted for intake of energy, there were no significant differences noted, indicating that the higher intake was due to an overall greater energy intake in boys. The MDI of MK-4 was significantly lower in children aged 5-8 years than in children aged 9-12 years, however, when adjusted for intake of energy, there was no significant difference between the age groups indicating that the higher intake was due to an overall greater energy intake in children aged 9-12 years.

Vitamin K_1 dietary sources in the NCFS II

Table 3 presents the contribution of food groups to the mean daily intake of vitamin K_1 in Irish children aged 5-12 years in the NCFS II (2017-18). ‘Vegetable & vegetable dishes’ was the key source of vitamin K_1 (28%), of which, ‘green vegetables’ accounted for 16%. ‘Meat & meat products’ contributed 17% of the MDI of vitamin K_1, of which, ‘meat dishes’ accounted for 10%. The contribution from ‘fruits’ and ‘potatoes & potato products’ to the MDI of vitamin K_1 was 11 and 8%, respectively.

MK-4 dietary sources in the NCFS II

Table 4 presents the contribution of food groups to the mean daily intake of MK-4 in Irish children aged 5-12 years in the NCFS II (2017-18). ‘Meat & meat products’ was the key source of MK-4 (60%), of which, ‘meat products’ and ‘fresh meat’ accounted for 27 and 20%, respectively. ‘Milk & yogurt’ contributed 16% of the MDI of MK-4. ‘Eggs & egg dishes’ and ‘cheese’ each contributed 6% of the MDI of MK-4.

MK-5-10 dietary sources in the NCFS II

Table 5 presents the contribution of food groups to the mean daily intake of MK-5-10 in Irish children aged 5-12 years in the NCFS II (2017-18). ‘Meat & meat products’ was the key source of MK-5-10 (46%), of which, ‘sausages’ accounted for 33%. ‘Cheese’ and ‘grains, rice, pasta & savouries’ contributed 32 and 11% of the MDI of MK-5-10, respectively.

Changes in the mean daily intake and sources of vitamin K_1 and vitamin K_2 between the NCFS II and the NCFS

Table 6 reports the mean daily intake of vitamin K_1 (µg/d & µg/kg/d) and vitamin K_2 (µg/d) (MK-4-10, MK-4 and MK-5-10) in Irish children aged 5-12 years in the NCFS II (2017-18) and the NCFS (2003-04). There were no differences in the MDI of vitamin K_1 or vitamin K_2 between children aged 5-12 years in the NCFS II and the NCFS.

Table 3 presents the contribution of food groups to the mean daily intake of vitamin K_1 in the NCFS II (2017-18) and the NCFS (2003-04). Overall, the key sources of vitamin K_1 in the NCFS II and the NCFS were ‘vegetable & vegetable dishes’, ‘meat & meat products’, ‘fruits’ and ‘potatoes & potato products’. ‘Vegetable & vegetable dishes’ was the key source of vitamin K_1 in both the NCFS II (28%) and the NCFS (29%), of which, ‘green vegetables’ contributed 16% of vitamin K_1 intake in both surveys. The contribution from ‘meat dishes’ and ‘fruits’ was higher in the NCFS II (10% and 11%, respectively) than the NCFS (5% and 7%, respectively). The contribution from ‘potatoes & potato products’ was lower in the NCFS II (8%) than the NCFS (15%).

Table 4 presents the contribution of food groups to the mean daily intake MK-4 in the NCFS II (2017-18) and the NCFS (2003-04). Overall, the key sources of MK-4 in the NCFS II and the NCFS were 'meat & meat products' and 'milk & yogurt'. 'Meat & meat products' was the key source of MK-4 in both the NCFS II (60%) and the NCFS (59%), of which, the contribution from 'meat products' was lower in the NCFS II (27%) than the NCFS (35%) and the contribution from 'fresh meat' was higher in the NCFS II (20%) than the NCFS (14%). The contribution from 'milk & yogurt' to the MDI of MK-4 was lower in the NCFS II (16%) than the NCFS (25%).

Table 5 presents the contribution of food groups to the mean daily intake of MK-5-10 in the NCFS II (2017-18) and the NCFS (2003-04). Overall, the key sources of MK-5-10 in the NCFS II and the NCFS were 'meat & meat products' and 'cheese'. While 'meat & meat products' was the key source of MK-5-10 in both surveys, the contribution was lower in the NCFS II (46%) than the NCFS (61%). Of the 'meat & meat products', 'sausages' contributed 33% of the MDI of MK-5-10 in the NCFS II and 51% in the NCFS. The contribution from 'cheese' was higher in the NCFS II (32%) than the NCFS (21%).

Table 1. Mean daily intake of vitamin K_1 (µg/d & µg/kg/d) in Irish children aged 5-12 years in the NCFS II (2017-18)

	Vitamin K_1 (µg/d)				Vitamin K_1 (µg/kg/d)			
	Mean	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**
All (*n* 600)	40.3	25.3	33.7	23.1-50.2	1.4	0.9	1.1	0.7-1.7
5-8 y (*n* 300)	38.9	24.2	32.7	22.3-48.9	1.6	1.1	1.4	0.9-2.1
9-12 y (*n* 300)	41.5	26.1	34.6	24.7-50.3	1.1*	0.7	0.9	0.6-1.4
Boys (*n* 300)	42.5	28.8	33.9	23.5-51.8	1.4	1.1	1.1	0.7-1.7
5-8 y (*n* 149)	41.0	28.3	32.7	22.3-50.6	1.7	1.2	1.3	0.9-2.1
9-12 y (n 151)	43.8	29.3	35.3	25.5-57.5	1.2	0.8	1.0	0.6-1.4
Girls (*n* 300)	37.9	20.7	33.7	22.6-49.2	1.3	0.8	1.1	0.7-1.7
5-8 y (*n* 151)	36.8	19.3	32.1	22.2-47.4	1.6	0.9	1.4	0.9-2.1
9-12 y (n 149)	39.1	22.0	34.5	23.5-49.9	1.0	0.6	0.9	0.6-1.3

No differences in intakes between boys and girls in µg/d (P=0.440) or µg/kg/d (P=0.465) via Mann-Whitney U Tests
Differences between age groups were assessed using a Kruscal Wallis test with differences denoted by different superscript lower case letters. At age 5-8 y intakes of vitamin K_1 (µg/kg/d) were significantly higher (P=0.000) than intakes at age 9-12 y

Table 2. Mean daily intake of MK-4-10, MK-4 and MK-5-10 (µg/d) in Irish children aged 5-12 years in the NCFS II (2017-18)

	MK-4-10 (µg/d)				**MK-4 (µg/d)**				**MK-5-10 (µg/d)**			
	Mean	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**
All (*n* 600)	47.8	48.5	27.8	14.8-68.5	9.6	5.0	8.7	6.0-12.3	38.2	44.8	20.4	7.0-57.1
5-8 y (*n* 300)	43.4	42.9	25.1	13.1-60.9	8.7	4.2	8.4	5.3-11.3	34.7	39.7	17.8	6.0-50.0
9-12 y (*n* 300)	51.8	53.0	31.0	15.9-73.5	10.4†	5.5	9.1	6.7-13.2	41.3	48.8	21.3	8.0-62.4
Boys (*n* 300)	53.3	51.9	35.2	15.4-75.4	10.5	5.4	9.8	6.7-13.2	42.9	47.9	26.6	8.0-62.2
5-8 y (*n* 149)	47.4	47.4	32.3	12.1-70.4	8.9	4.3	8.8	5.4-11.6	38.5	40.2	26.0	5.5-59.0
9-12 y (n 151)	58.5	58.0	35.7	19.1-80.7	11.8	6.0	11.1	7.5-14.5	46.7	53.5	27.3	8.6-68.0
Girls (*n* 300)	41.9	44.0	23.6	13.1-57.6	8.7*	4.3	7.9	5.6-10.9	33.2	40.7	15.7	6.0-48.0
5-8 y (*n* 151)	39.4	42.1	22.4	13.6-50.3	8.4	4.1	7.8	5.2-10.9	31.0	39.1	15.5	6.6-41.9
9-12 y (n 149)	44.3	45.8	24.2	12.3-71.6	8.9	4.5	8.0	5.8-10.9	35.4	42.3	15.9	5.5-61.3

*Significantly different (P=0.000) from that of boys within the column via Mann Whitney U Tests

† Significantly different (P=0.000) from that of 5-8 y age group within the column via Kruskal Wallis Test

Table 3. Contribution (µg & %) of food groups to the mean daily intake of vitamin K_1 in Irish children aged 5-12 years in the NCFS II (2017-18) and the NCFS (2003-04)

	NCFS II (*n* 600)		**NCFS (*n* 594)**	
Food groups	**µg**	**%**	**µg**	**%**
Vegetable & vegetable dishes	**14.5**	**27.9**	**16.0**	**29.3**
Green vegetables	*9.3*	*15.5*	*9.3*	*15.8*
Other vegetables	*2.9*	*6.6*	*2.5*	*5.2*
Peas, beans & lentils	*1.5*	*3.9*	*1.5*	*4.3*
Vegetable & pulse dishes	*0.8*	*1.8*	*2.7*	*4.0*
Meat & meat products	**6.7**	**17.3**	**4.0**	**11.4**
Meat dishes	*4.3*	*9.8*	*1.8*	*4.8*
Meat products (sausages, burgers, meat pies)	*1.8*	*5.5*	*2.0*	*6.1*
Fresh meat	*0.6*	*2.0*	*0.1*	*0.4*
Fruit & fruit juices	**4.3**	**11.8**	**2.8**	**7.4**
Fruits	*4.0*	*11.1*	*2.7*	*7.0*
Fruit juices & smoothies	*0.2*	*0.7*	*0.1*	*0.4*
Potatoes & potato products	2.7	8.2	4.9	15.0
Biscuits, cakes & pastries	2.1	5.8	1.6	4.8
Butter, spreading fats & oils	1.7	5.5	3.1	9.4
Soups, sauces & miscellaneous foods	1.8	4.0	1.0	2.5
Milk & yogurt	1.0	3.4	1.6	5.3
Grains, rice, pasta & savouries	1.1	3.1	0.8	2.3
Sugars, confectionery, preserves & savoury snacks	1.0	3.1	1.7	5.5
Bread & rolls	0.8	2.6	0.7	2.0
Fish & fish dishes	0.8	2.0	0.4	1.0
Breakfast cereals	0.5	1.7	0.4	1.3
Cheese	0.4	1.2	0.2	0.8
Creams, ice-creams & chilled desserts	0.3	1.1	0.4	1.0
Eggs & egg dishes	0.2	0.5	0.2	0.6
Beverages	0.1	0.3	0.1	0.3
Nutritional supplements	0.2	0.3	0.0	0.0
Nuts, seeds, herbs & spices	0.1	0.3	0.1	0.2
Total	**40.3**	**100**	**39.9**	**100**

Table 4. Contribution (µg & %) of food groups to the mean daily intake of MK-4 in Irish children aged 5-12 years in the NCFS II (2017-18) and the NCFS (2003-04)

	NCFS II (*n* 600)		**NCFS (*n* 594)**	
Food groups	**µg**	**%**	**µg**	**%**
Meat & meat products	**6.1**	**59.8**	**6.3**	**59.0**
Meat products (sausages, burgers, meat pies)	*3.1*	*27.3*	*4.0*	*35.3*
Fresh meat	*1.9*	*20.2*	*1.4*	*14.1*
Meat dishes	*1.1*	*12.3*	*0.9*	*9.5*
Milk & yogurt	**1.4**	**15.5**	**2.3**	**24.5**
Eggs & egg dishes	**0.6**	**6.1**	**0.5**	**4.7**
Cheese	0.4	5.5	0.3	3.6
Butter, spreading fats & oils	0.4	4.7	0.3	2.5
Creams, ice-creams & chilled desserts	0.2	1.9	0.2	2.2
Breakfast cereals	0.1	1.4	0.0	0.0
Grains, rice, pasta & savouries	0.1	1.4	0.0	0.6
Sugars, confectionery, preserves & savoury snacks	0.1	1.3	0.2	1.9
Potatoes & potato products	0.1	1.2	0.1	0.9
Fish & fish dishes	0.0	0.5	0.0	0.2
Biscuits, cakes & pastries	0.0	0.3	0.0	0.0
Bread & rolls	0.0	0.2	0.0	0.0
Vegetable & vegetable dishes	0.0	0.1	0.0	0.1
Fruit & fruit juices	0.0	0.1	0.0	0.0
Beverages	0.0	0.0	0.0	0.0
Soups, sauces & miscellaneous foods	0.0	0.1	0.0	0.0
Nutritional supplements	0.0	0.0	0.0	0.0
Nuts, seeds, herbs & spices	0.0	0.0	0.0	0.0
Total	**9.6**	**100**	**10.1**	**100**

Table 5. Contribution (µg & %) of food groups to the mean daily intake of MK-5-10 in Irish children aged 5-12 years in the NCFS II (2017-18) and the NCFS (2003-04)

	NCFS II (*n* 600)		**NCFS (*n* 594)**	
Food groups	**µg**	**%**	**µg**	**%**
Meat & meat products	**29.0**	**45.6**	**35.3**	**61.2**
Sausages	*25.9*	*33.0*	*33.0*	*51.1*
Fresh meat	*0.3*	*4.7*	*0.2*	*2.8*
Meat dishes	*1.0*	*3.9*	*0.7*	*1.8*
Meat products (burgers, meat pies)	*1.8*	*3.9*	*1.4*	*5.6*
Cheese	**6.8**	**31.9**	**4.8**	**20.9**
Grains, rice, pasta & savouries	**1.7**	**11.2**	**1.1**	**8.9**
Milk & yogurt	0.2	6.3	0.4	6.8
Fish & fish dishes	0.1	1.6	0.1	0.8
Bread & rolls	0.1	1.1	0.0	0.0
Creams, ice-creams & chilled desserts	0.1	0.7	0.0	0.4
Eggs & egg dishes	0.2	0.5	0.1	0.5
Butter, spreading fats & oils	0.0	0.4	0.0	0.2
Breakfast cereals	0.0	0.3	0.0	0.0
Nutritional supplements	0.0	0.2	0.0	0.0
Vegetable & vegetable dishes	0.0	0.2	0.0	0.2
Biscuits, cakes & pastries	0.0	0.0	0.0	0.0
Potatoes & potato products	0.0	0.0	0.0	0.1
Fruit & fruit juices	0.0	0.0	0.0	0.0
Beverages	0.0	0.0	0.0	0.0
Sugars, confectionery, preserves & savoury snacks	0.0	0.0	0.0	0.0
Soups, sauces & miscellaneous foods	0.0	0.0	0.0	0.0
Nuts, seeds, herbs & spices	0.0	0.0	0.0	0.0
Total	**38.2**	**100**	**41.7**	**100**

Table 6. Mean daily intake of vitamin K_1 (µg/d & µg/kg/d) and vitamin K_2 (µg/d) (MK-4-10, MK-4 and MK-5-10) in Irish children aged 5-12 years in the NCFS II (2017-18) and the NCFS (2003-04)

	NCFS II (*n* 600)				**NCFS (*n* 594)**			
	Mean	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**
Vitamin K_1 (µg/d)	40.3	25.3	33.7	23.1-50.2	39.9	23.8	33.2	24.3-49.2
Vitamin K_1 (µg/kg/d)	1.4	0.9	1.1	0.7-1.7	1.3	0.8	1.1	0.8-1.6
MK-4-10 (µg/d)	47.8	48.5	27.8	14.8-68.5	51.8	46.9	38.9	17.3-71.1
MK-4 (µg/d)	9.6	5.0	8.7	6.0-12.3	10.1	4.4	9.5	6.8-12.2
MK-5-10 (µg/d)	38.2	44.8	20.4	7.0-57.1	41.7	43.4	29.8	8.7-59.4

There were no differences ($P<0.01$) in intakes between the NCFS II and NCFS via Mann Whitney U Tests

Discussion

The aim of this chapter was to estimate the current intake and sources of vitamin K_1 and vitamin K_2 in Irish school-aged children from the NCFS II (2017-18) and to identify any changes in vitamin K_1 and vitamin K_2 intake and sources since the previous NCFS (2003-2004). The MDI of vitamin K_1 in the NCFS II was 1.4µg/kg/d, with 'vegetable & vegetable dishes', 'meat & meat products' and 'fruits' the key sources of vitamin K_1 accounting for 28, 17 and 11% of intakes, respectively. The MDI of MK-4-10 was 48µg/d (MK-4: 10µg/d, MK-5-10: 38µg/d). 'Meat & meat products' and 'milk & yogurt' were the key sources of MK-4 in Irish children accounting for 60 and 16% of intakes, respectively. 'Meat & meat products' and 'cheese' were the key sources of MK-5-10 in Irish children accounting for 46 and 32% of intakes, respectively. There was no difference in the MDI or key dietary sources of vitamin K_1 or vitamin K_2 between the current NCFS II (2017-18) and the NCFS (2003-04).

In the NCFS II, mean daily vitamin K_1 intake was above the EFSA AI of 1µg/kg/d for each gender and age group examined (EFSA Panel on Dietetic Products *et al.*, 2017). The MDI of vitamin K_1 in Irish children (40µg/d) was lower than intakes reported in national surveys of children in Austria (59-75µg/d for children aged 7-12 years) and the United States (63µg/d for children 6-11 years) (Elmadfa *et al.*, 2012, US Department of Agriculture, 2018). The higher consumption of fruit and vegetables in Austrian children (265g) compared to Irish children (221g) may partly explain the higher intake of vitamin K_1 observed in Austrian children (Yngve *et al.*, 2005, Irish Universities Nutrition Alliance, 2019). The inclusion of french fries as a vegetable in the American dietary guidelines and the frequent consumption of fried potato products in American children may contribute somewhat to the higher vitamin K_1 intakes observed in American children due to the vitamin K_1 rich oils which may be used in the cooking and preparation of potato products (Peterson *et al.*, 2002, Lorson *et al.*, 2009, McGuire, 2011).

'Vegetable & vegetable dishes' (28%) was the key source of vitamin K_1 in Irish children, of which, 'green vegetables' accounted for 16%. Similar findings have been reported in children in the US and the UK with green vegetables contributing 15-35% of vitamin K_1 intake (Booth *et al.*, 1996, Prynne *et al.*, 2005). 'Meat & meat products' contributed 17% of vitamin K_1 intake, of which, 'meat dishes' accounted for 10%. Mixed dishes have previously been reported as an unexpected source of vitamin K and a key contributor to vitamin K_1 intakes in the US primarily due to the oils and vegetables included in the dish (Finnan *et al.*, 2017, Harshman *et al.*, 2017). The contribution from 'fruits' (11%) was due the consumption of whole fruits some of which contain moderate amounts of vitamin K_1 (e.g. Kiwi fruit, berries) (Dismore *et al.*, 2003).

For vitamin K_2, the MDI of MK-4-10 was 48µg/d in Irish children aged 5-12 years, with mean intakes of MK-4 and MK-5-10 of 10 and 38µg/d, respectively. As there is currently no dietary reference value for vitamin K_2, no statement can be made on the adequacy of these intakes (EFSA Panel on Dietetic Products *et al.*, 2017).

'Meat & meat products' accounted for almost 60% of the MDI of MK-4 in Irish children followed by 'milk and yogurt' which accounted for 16% of intakes. MK-4 found in these foods is as a result of the menadione added to animal feed or the conversion from ingested vitamin K_1 in mammals (Hirota *et al.*, 2013, EFSA Panel on Additives and Products or Substances used in Animal Feed, 2014).

The key source of MK-5-10 in Irish children was 'meat & meat products' (46%), of which, 'sausages' accounted for 33% of intakes, which is explained by the high menaquinone concentration in sausages (336µg/100g) (Fu *et al.*, 2016). 'Cheese' contributed 32% of MK-5-10 intake in Irish children. The origin of these menaquinones is due to the starter culture used in the fermentation process and cheese has been outlined as one of the most important sources of the long chain menaquinones in the Western Diet (Vermeer *et al.*, 2018).

Changes in the intakes and sources of vitamin K_1 and vitamin K_2 between the NCFS II and the NCFS

When comparing the MDI of vitamin K_1 in the NCFS II (2017-18) and the NCFS (2003-04), there was no difference (P=0.440) in intake between the two surveys (1.4µg/kg/d v 1.3µg/kg/d). 'Vegetable & vegetable dishes' was the key food group contributing to vitamin K_1 intake in both surveys (28% v 29%), of which 'green vegetables' contributed 16% in both surveys. While 'meat & meat products', 'fruits' and 'potatoes & potato products' were also key sources of vitamin K_1 in both surveys, changes in the relative contribution of these food groups are reflective of the changes in dietary patterns observed since the NCFS (Irish Universities

Nutrition Alliance, 2019). The contribution from ‘meat & meat products’ and ‘fruits’ was higher in the NCFS II (17% and 12%, respectively) than the NCFS (11% and 7%, respectively). This was attributable to the higher consumption of ‘meat dishes’ (47g) and ‘discrete fruit’ (90g) in the NCFS II compared to the NCFS (37g and 59g, respectively) (Irish Universities Nutrition Alliance, 2019). There was a lower contribution to vitamin K_1 from ‘potatoes & potato products’ in the NCFS II (8%) than the NCFS (15%), due to a lower intake of this food group in the NCFS II (61g) compared to the NCFS (98g).

There are a small number of studies reporting the key food groups contributing to intakes of vitamin K_1 in children. Prynne *et al.* (2005) reported that ‘vegetable and vegetable products’ contributed 48% of vitamin K_1 intake in British children aged 4 years, of which, 15% came from ‘green leafy vegetables’. ‘Potato and potato products’ accounted for 18% of intakes in British children which is far higher than the 8% contribution in Irish children in the NCFS II. Variances in the foods included in the ‘potato and potato products’ food group and differences in the age categories may partly explain the large difference in the contribution between British children and Irish children. Additional foods may have been included that are not outlined. Similarly, data from the Food and Drug Administrations Total Diet Study in the US (1987-88) reported that green vegetables were the top contributor to vitamin K_1 intake (26-35%) across each gender and age group from 2-16 years (Booth *et al.*, 1996).

There were no differences in the MDI of MK-4-10, MK-4 and MK-5-10 between the NCFS II (2017-18) and the NCFS (2003-04) of Irish children aged 5-12 years. ‘Meat and meat products’ was the key source of MK-4 in both the NCFS II (60%) and the NCFS (59%). However, there was a lower contribution from ‘meat products’ in the NCFS II (27%) compared to the NCFS (35%) and a higher contribution from ‘fresh meat’ in the NCFS II (20%) than the NCFS (14%). There was a lower contribution from ‘milk & yogurt’ in the NCFS II (16%) compared to the NCFS (25%) due to a lower consumption of milk in the NCFS II (186g) than the NCFS (258g).

The contribution from ‘meat & meat products’ to intakes of MK-5-10 was lower in the NCFS II (46%) than the NCFS (61%) primarily due to the lower consumption of ‘sausages’ in the NCFS II (28g v 19g) (Irish Universities Nutrition Alliance, 2019). The contribution from ‘cheese’ to the MDI of MK-5-10 was 32% in the NCFS II and 21% in the NCFS reflective of the slightly higher consumption of cheese in the NCFS II (11g v 8g).

There are currently no nationally representative data on the key sources of vitamin K_2 in children across Europe or the US. In adults, the sources of menaquinones were reported in two studies which used dietary data from the EPIC study with dairy products (60%), especially cheese (43-53%), and meat and meat products (17%) found to be the key contributors to intakes of the menaquinones (Nimptsch *et al.*, 2008, Beulens *et al.*, 2010). Further research is needed to examine the key sources of vitamin K_2 in children across Europe and further afield.

Public health implication

Although the intake of vitamin K_1 in Irish children was higher than the AI required to maintain normal blood coagulation (EFSA Panel on Dietetic Products *et al.*, 2017), evidence suggests that current dietary reference values may be insufficient to support the role of vitamin K in extra hepatic functions such as the carboxylation of osteocalcin (McCann and Ames, 2009). For example, high levels of undercarboxylated osteocalcin and a poor vitamin K status of bone during growth have been reported in children in the Netherlands (Van Summeren *et al.*, 2007, Van Summeren *et al.*, 2008). In addition, children with an unfavourable ratio of undercarboxylated osteocalcin to carboxylated osteocalcin (UCR) have a 78 times greater risk of low energy fractures (fall from the child’s own height or a fall during team games) (Popko *et al.*, 2018). Considering improvements in the UCR have been reported in children supplemented with MK-7 (Van Summeren *et al.*, 2009) and a better vitamin K status results in improvements in bone health parameters (Kalkwarf *et al.*, 2004, O'Connor *et al.*, 2007, Van Summeren *et al.*, 2008); further research is required to investigate if current dietary reference values support the role of vitamin K beyond its function in haemostasis.

Strengths and limitations

The key strength of this study was the high quality dietary data (including brand and recipe level data) used to estimate vitamin K_1 and vitamin K_2 intakes and sources in both the NCFS II and the NCFS, both of which had a similar methodology allowing direct comparison between the two surveys. The issue of under reporting, a known limitation with all dietary assessment, was minimised by high level of researcher-participant interaction by trained research nutritionists.

Conclusion

This was the first study to estimate changes in the intakes and dietary sources of vitamin K_1 and vitamin K_2 using nationally representative samples of children. The key finding was that the mean daily intake of vitamin K_1 in Irish children aged 5-12 years from the NCFS II was above the EFSA AI of 1.0µg/kg/d for all gender and age groups examined. ‘Vegetable & vegetable dishes’ ‘meat & meat products’ and ‘fruits’ were the key sources of vitamin K_1. The mean daily intake of MK-4-10 was 48µg/d, with mean intakes of MK-4 and MK-5-10 of 10 and 38µg/d, respectively. ‘Meat & meat products’ ‘cheese’ and ‘milk & yogurt’ were key sources of menaquinones in Irish children in the NCFS II.

There were no differences observed in vitamin K_1 and vitamin K_2 intakes between the NCFS II (2017-18) and the NCFS (2003-04). Furthermore, the key sources of both vitamin K_1 and vitamin K_2 were similar between the two surveys however, there were some slight differences in the relative contribution of food groups to vitamin K intakes explained by changes in dietary patterns over the last 15 years. Considering that current dietary intakes of vitamin K may not support the carboxylation of the extra hepatic vitamin K dependent proteins, food based strategies may be required to increase vitamin K intakes in children.

References

Beulens, J. W., van der, A. D., Grobbee, D. E., Sluijs, I., Spijkerman, A. M. & van der Schouw, Y. T. (2010). Dietary phylloquinone and menaquinones intakes and risk of type 2 diabetes. *Diabetes Care,* 33**,** 1699-705.

Bolton-Smith, C., Price, R. J., Fenton, S. T., Harrington, D. J. & Shearer, M. J. (2000). Compilation of a provisional UK database for the phylloquinone (vitamin K1) content of foods. *British Journal of Nutrition,* 83**,** 389-99.

Booth, S. L., Pennington, J. A. & Sadowski, J. A. (1996). Food sources and dietary intakes of vitamin K-1 (phylloquinone) in the American diet: data from the FDA Total Diet Study. *Journal of the American Dietetic Association,* 96**,** 149-54.

Booth, S. L., Sadowski, J. A., Weihrauch, J. L. & Ferland, G. (1993). Vitamin K1 (Phylloquinone) Content of Foods: A Provisional Table. *Journal of Food Composition and Analysis,* 6**,** 109-120.

Damon, M., Zhang, N. Z., Haytowitz, D. B. & Booth, S. L. (2005). Phylloquinone (vitamin K1) content of vegetables. *Journal of Food Composition and Analysis,* 18**,** 751-758.

Dismore, M. L., Haytowitz, D. B., Gebhardt, S. E., Peterson, J. W. & Booth, S. L. (2003). Vitamin K content of nuts and fruits in the US diet. *Journal of the American Dietetic Association,* 103**,** 1650-2.

EFSA Panel on Additives and Products or Substances used in Animal Feed (2014). Scientific Opinion on the safety and efficacy of vitamin K3 (menadione sodium bisulphite and menadione nicotinamide bisulphite) as a feed additive for all animal species. *EFSA Journal,* 12**,** 3532.

EFSA Panel on Dietetic Products, N., Allergies, Turck, D., Bresson, J.-L., Burlingame, B., Dean, T., Fairweather-Tait, S., Heinonen, M., Hirsch-Ernst, K. I., Mangelsdorf, I., McArdle, H. J., Naska, A., Nowicka, G., Pentieva, K., Sanz, Y., Siani, A., Sjödin, A., Stern, M., Tomé, D., Van Loveren, H., Vinceti, M., Willatts, P., Lamberg-Allardt, C., Przyrembel, H., Tetens, I., Dumas, C., Fabiani, L., Ioannidou, S. & Neuhäuser-Berthold, M. (2017). Dietary reference values for vitamin K. *EFSA Journal,* 15**,** e04780.

Elmadfa, I., Hasenegger, V., Wagner, K., Putz, P., Weidl, N.-M., Wottawa, D., Kuen, T., Seiringer, G., Meyer, A., Sturtzel, B., Kiefer, I., Zilberszac, A., Sgarabottolo, V., Meidlinger, B. & Rieder, A. (2012). Österreichischer Ernährungsbericht 2012.

Fagerland, M. W. (2012). t-tests, non-parametric tests, and large studies—a paradox of statistical practice? *BMC Medical Research Methodology,* 12**,** 78.

Finnan, E. G., Harshman, S. G., Haytowitz, D. B. & Booth, S. L. (2017). Mixed dishes are an unexpected source of dietary vitamin K. *Journal of Food Composition and Analysis,* 64**,** 127-131.

Food Standards Agency (2002). Food Portion Sizes. London: The Stationary Office.

Foster, E., Hawkins, A. & Adamson, A. 2010. *Young Person's Food Atlas: Primary,* England, Food Standards Agency.

Fu, X., Shen, X., Finnan, E. G., Haytowitz, D. B. & Booth, S. L. (2016). Measurement of Multiple Vitamin K Forms in Processed and Fresh-Cut Pork Products in the U.S. Food Supply. *Journal of Agricultural and Food Chemistry,* 64**,** 4531-5.

Harshman, S. G., Finnan, E. G., Barger, K. J., Bailey, R. L., Haytowitz, D. B., Gilhooly, C. H. & Booth, S. L. (2017). Vegetables and Mixed Dishes Are Top Contributors to Phylloquinone Intake in US Adults: Data from the 2011-2012 NHANES. *Journal of Nutrition,* 147**,** 1308-1313.

Hirota, Y., Tsugawa, N., Nakagawa, K., Suhara, Y., Tanaka, K., Uchino, Y., Takeuchi, A., Sawada, N., Kamao, M., Wada, A., Okitsu, T. & Okano, T. (2013). Menadione (vitamin K3) is a catabolic product of oral phylloquinone (vitamin K1) in the intestine and a circulating precursor of tissue menaquinone-4 (vitamin K2) in rats. *Journal of Biological Chemistry,* 288**,** 33071-80.

Irish Universities Nutrition Alliance (2019). *National Children's Food Survey II: Summary report on Food and Nutrient Intakes, Body Weight, Physical Activity and Eating Behaviours in Children Aged 5-12 Years in Ireland*

Kalkwarf, H. J., Khoury, J. C., Bean, J. & Elliot, J. G. (2004). Vitamin K, bone turnover, and bone mass in girls. *American Journal of Clinical Nutrition,* 80**,** 1075-80.

Krebs-Smith, S. M., Kott, P. S. & Guenther, P. M. (1989). Mean proportion and population proportion: two answers to the same question? *Journal of the American Dietetic Association,* 89**,** 671-6.

Lorson, B. A., Melgar-Quinonez, H. R. & Taylor, C. A. (2009). Correlates of Fruit and Vegetable Intakes in US Children. *Journal of the American Dietetic Association,* 109**,** 474-478.

Lyons, J., Walton, J. & Flynn, A. (2013). Development of an online database of typical food portion sizes in Irish population groups. *Journal of nutritional science,* 2**,** e25-e25.

McCann, J. C. & Ames, B. N. (2009). Vitamin K, an example of triage theory: is micronutrient inadequacy linked to diseases of aging? *American Journal of Clinical Nutrition,* 90**,** 889-907.

McGuire, S. (2011). U.S. Department of Agriculture and U.S. Department of Health and Human Services, Dietary Guidelines for Americans, 2010. 7th Edition, Washington, DC: U.S. Government Printing Office, January 2011. *Advances in Nutrition,* 2**,** 293-4.

Nimptsch, K., Rohrmann, S. & Linseisen, J. (2008). Dietary intake of vitamin K and risk of prostate cancer in the Heidelberg cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC-Heidelberg). *American Journal of Clinical Nutrition,* 87**,** 985-92.

O'Connor, E., Molgaard, C., Michaelsen, K. F., Jakobsen, J., Lamberg-Allardt, C. J. & Cashman, K. D. (2007). Serum percentage undercarboxylated osteocalcin, a sensitive measure of vitamin K status, and its relationship to bone health indices in Danish girls. *British Journal of Nutrition,* 97**,** 661-6.

Peterson, J. W., Muzzey, K. L., Haytowitz, D., Exler, J., Lemar, L. & Booth, S. L. (2002). Phylloquinone (vitamin K1) and dihydrophylloquinone content of fats and oils. *Journal of the American Oil Chemists' Society,* 79**,** 641-646.

Popko, J., Karpinski, M., Chojnowska, S., Maresz, K., Milewski, R., Badmaev, V. & Schurgers, L. J. (2018). Decreased Levels of Circulating Carboxylated Osteocalcin in Children with Low Energy Fractures: A Pilot Study. *Nutrients,* 10.

Presse, N., Potvin, S., Bertrand, B., Calvo, M. S. & Ferland, G. (2015). Phylloquinone content of herbs, spices and seasonings. *Journal of Food Composition and Analysis,* 41**,** 15-20.

Prynne, C. J., Thane, C. W., Prentice, A. & Wadsworth, M. E. (2005). Intake and sources of phylloquinone (vitamin K(1)) in 4-year-old British children:

comparison between 1950 and the 1990s. *Public Health Nutrition,* 8**,** 171-80.

Public Health England Composition of Foods Integrated Dataset. 2015. *McCance and Widdowson's The Composition of Foods Integrated Dataset 2015* [Online]. Available: https://www.gov.uk/government/publications/composition-of-foods-integrated-dataset-cofid.

Schurgers, L. J. & Vermeer, C. (2000). Determination of phylloquinone and menaquinones in food. Effect of food matrix on circulating vitamin K concentrations. *Haemostasis,* 30**,** 298-307.

US Department of Agriculture (2018). Nutrient Intakes from Food and Beverages: Mean amounts consumed per Individual , by Gender and Age, What we eat in America, NHANES 2015-2016.

USDA National Nutrient Database for Standard References Release 28. 2015. Washington (DC): USDA Agricultural Research Service. Available: http://www.ars.usda.gov/nutrientdata [Accessed January 2016].

Van Summeren, M., Braam, L., Noirt, F., Kuis, W. & Vermeer, C. (2007). Pronounced elevation of undercarboxylated osteocalcin in healthy children. *Pediatric Research,* 61**,** 366-70.

Van Summeren, M. J., Braam, L. A., Lilien, M. R., Schurgers, L. J., Kuis, W. & Vermeer, C. (2009). The effect of menaquinone-7 (vitamin K2) supplementation on osteocalcin carboxylation in healthy prepubertal children. *British Journal of Nutrition,* 102.

Van Summeren, M. J., van Coeverden, S. C., Schurgers, L. J., Braam, L. A., Noirt, F., Uiterwaal, C. S., Kuis, W. & Vermeer, C. (2008). Vitamin K status is associated with childhood bone mineral content. *British Journal of Nutrition,* 100**,** 852-8.

Vermeer, C., Raes, J., van 't Hoofd, C., Knapen, M. H. J. & Xanthoulea, S. (2018). Menaquinone Content of Cheese. *Nutrients,* 10.

Yngve, A., Wolf, A., Poortvliet, E., Elmadfa, I., Brug, J., Ehrenblad, B., Franchini, B., Haraldsdóttir, J., Krølner, R., Maes, L., Pérez-Rodrigo, C., Sjöström, M., Thórsdóttir, I. & Klepp, K. I. (2005). Fruit and Vegetable Intake in a Sample of 11-Year-Old Children in 9 European Countries: The Pro Children Cross-Sectional Survey. *Annals of Nutrition and Metabolism,* 49**,** 236-245.

Chapter 7

General Discussion

The role of vitamin K in maintaining normal blood coagulation is well established however, on-going research has suggested that vitamin K may have a further role in areas such as bone health, cardiovascular health, cognition and anti-inflammatory functions (Booth, 2009, Vermeer and Theuwissen, 2011, Halder *et al.*, 2019, Simes *et al.*, 2020). There are currently few data available on vitamin K intakes in nationally representative samples of population groups (partly due to limited composition data for vitamin K and its individual components) and the European Food Safety Authority (EFSA) have recently outlined the need for further data on the intake of vitamin K (including phylloquinone and menaquinones) in European population groups (EFSA Panel on Dietetic Products *et al.*, 2017). In direct response to this call from the EFSA, this PhD thesis aimed to estimate the intake, adequacy and dietary sources of vitamin K_1 and vitamin K_2 in nationally representative samples of the Irish population aged 1-90 years. A further aim was to investigate any changes in vitamin K_1 and vitamin K_2 intakes and sources in school-aged children between 2003-04 and 2017-18 using data from two nationally representative surveys of Irish children (5-12y), which used similar methodologies for dietary assessment. To facilitate estimation of these intakes, the first step of this thesis was to update the Irish Food Composition Database with composition data for vitamin K_1 and vitamin K_2.

The Irish Food Composition Database (IFCD) (2012) contains comprehensive data for 3443 foods and beverages consumed by the Irish population aged 1-90 years, collected during four national dietary surveys carried out by the Irish Universities Nutrition Alliance over the last 20 years. These surveys included the National Pre-school Nutrition Survey (1-4y) (2010-11), the National Children's Food Survey (5-12y) (2003-04), the National Teens' Food Survey (13-17y) (2005-06) and the National Adult Nutrition Survey (18-90y) (2008-10) (www.iuna.net). As the IFCD (2012) only contains limited data for vitamin K_1 and no data for vitamin K_2, the first aim of this thesis was to update the IFCD (2012) with composition data for vitamin K_1 and vitamin K_2 (menaquinone-4 (MK-4) and menaquinone-5-10 (MK-10)). As there are no analytical composition data available for the vitamin K_1 or vitamin K_2 content of foods in Ireland, composition data were obtained or 'borrowed' from other analytical sources as this is considered to be an appropriate method for estimating nutrient content when direct analysis is not feasible (Rand *et al.*, 1991, Schakel *et al.*, 1997).

For vitamin K_1, published analytical values from the UK Composition of Foods Integrated Dataset (COFID) and the United States Department of Agriculture (USDA) National Nutrient Database provided composition data for 48% of food codes and analytical values sourced from published papers provided composition data for a further 5% of food codes (Booth *et al.*, 1993, Bolton-Smith *et al.*, 2000, Dismore *et al.*, 2003, Damon *et al.*, 2005, Presse *et al.*, 2015, Public Health England Composition of Foods Integrated Dataset, 2015, USDA National Nutrient Database for Standard References Release 28, 2015). Composition data from these sources were also used to estimate the vitamin K_1 content of recipes of composite dishes which were calculated at ingredient level and made up almost one third (31%) of all food codes in the IFCD (2012). This was necessary to account for the large variation in the vitamin K_1 content of certain foods such as cooking oils and vegetables, both of which are common ingredients of composite dishes and this methodology can be considered a key strength of the present study (Peterson et al., 2002, Damon et al., 2005).

In general, foods in the IFCD (2012) were not fortified with vitamin $K_{1,}$ with the notable exception of infant formula. Furthermore, most nutritional supplements did not contain vitamin $K_{1.}$ For those retail products/supplements that did contain vitamin K_1, nutritional information from product labels (at brand level) was used to assign appropriate vitamin K_1 values. For a small number of food codes, the vitamin K_1 content was assigned based on the fat content of a similar product or where no composition data were available, foods were assigned a value of zero as they were likely to contain negligible amounts of vitamin K_1. Herbs (213-3220µg/100g) and 'vegetable & vegetable dishes' (0-840µg/100g) were the most concentrated foods with vitamin K_1 in the database. Hence, in order to ensure accurate estimates of vitamin K_1 intakes in the Irish population, herbs in quantities as low as 0.5g in recipes of composite dishes were included when assigning vitamin K_1 values to foods in the IFCD (2012).

For vitamin $K_{2,}$ the IFCD (2012) was also updated to include MK-4 and MK-5-10 composition data for the 3443 food codes. The menaquinones are produced by bacteria capable of food fermentation (with the exception of MK-4), and are therefore found in foods of animal origin and fermented foods (Schurgers and Vermeer, 2000, Manoury *et al.*, 2013, Tarvainen *et al.*, 2019). The amount and types of menaquinones present in a food are dependent on the fermentation conditions and the form of bacteria used in the production process (Walther and Chollet, 2017). MK-4 differs from the other menaquinones as it is not produced by bacteria but is formed in mammals from the tissue specific conversion from ingested vitamin K_1 or menadione (a synthetic form of vitamin K added to animal feed) (Okano *et al.*, 2008, Hirota *et al.*, 2013, EFSA Panel on Additives and Products or Substances used in Animal Feed, 2014). When updating the IFCD (2012) for menaquinones, foods that were either not fermented or were not of animal origin (48% of food codes) were assigned a 0µg value for MK-4 and MK-5-10. Published analytical values from the UK COFID and published papers provided composition data for 16% of food codes (Schurgers and Vermeer, 2000, Public Health England Composition of Foods Integrated Dataset, 2015, Fu *et al.*, 2016). Using a similar methodology to that used to assign vitamin K_1 values to recipes, the MK-4 and MK-5-10 content of recipes of composite dishes in the IFCD (2012) were calculated at ingredient level (25% of food codes). Using nutritional information on product labels (at brand level), it was found that there were no foods or nutritional supplements in the database that were fortified with either MK-4 or MK-5-10 hence they were assigned a 0µg value for MK-4 and MK-5-10. A composition value of zero was assigned to a small number (<1%) of food codes where there were no composition data available. Foods highest in MK-4 were 'meat & meat products' (0-28µg/100g), 'eggs & egg dishes' (2.2-15µg/100g) and 'butter, spreading fats & oils' (0-15µg/100g). Foods highest in MK-5-10 were 'meat & meat products' (0-341µg/100g), 'cheese' (24-72µg/100g) and 'eggs & egg dishes' (0-28µg/100g). Given the high vitamin K_2 concentration of these products and the wide consumption in the Irish population, they are likely to make significant contributions to intakes of vitamin K_2. The composition data for vitamin K (including phylloquinone and menaquinones) now available in IFCD (2012) is the first to provide data on the vitamin K composition of foods in Ireland. This database will support the assessment of vitamin K_1 and vitamin K_2 intakes across the Irish population.

Few national dietary surveys have estimated vitamin K intake in population groups, which may be partly due to the limited composition data for vitamin K and its separate components (Shearer and Bolton-Smith, 2000, Elmadfa and Meyer, 2010). In Ireland, the intake of vitamin K_1 in adults aged 18-90 years has previously been published, (Hayes *et al.*, 2016) however there are no data published on intakes of vitamin K_1 in other population groups (with the exception of preliminary estimates for children aged

5-12y using limited food composition data) (Hannon *et al.*, 2007). Therefore, the next aim of this thesis was to estimate the intake, adequacy and sources of vitamin K_1 in Irish children aged 1-17 years. The current study used dietary data from three nationally representative surveys of Irish children; the National Pre-school Nutrition Survey of young children (1-4y), the National Children's Food Survey of school-aged children (5-12y) and the National Teens' Food Survey of adolescents (13-17y). The key finding of this study was that the mean intakes of vitamin K_1 for Irish pre-school children (2.2µg/kg/d) and school-aged children (1.3µg/kg/d) were above the EFSA Adequate Intake (AI) of 1µg/kg/d (required to maintain normal blood coagulation), however the mean vitamin K_1 intake for Irish teenagers (0.9µg/kg/d) was below the same AI (EFSA Panel on Dietetic Products et al., 2017). Vitamin K_1 intake in Irish pre-school children was similar to vitamin K intakes in children aged 1-5 years in Greece (32µg/d) and higher than vitamin K_1 intake in 4-year-old children in the UK (1.4µg/kg/day) (Prynne *et al.*, 2005, Manios *et al.*, 2008). Vitamin K_1 intakes in Irish school-aged children (40µg/d) and teenagers (55µg/d) were generally lower than intakes reported in nationally representative samples of Austrian children 7-14y (59-75µg/d) and US children 6-19y (63-79µg/d) (Elmadfa *et al.*, 2012, US Department of Agriculture, 2018). This may be somewhat attributable to differences in food consumption patterns or food-based dietary guidelines between countries, such as the higher consumption of fruit and vegetables reported in Austrian Children (Yngve *et al.*, 2005) and the inclusion of french fries (in the vegetable food-group) in the American dietary guidelines (McGuire, 2011).

In the present study of Irish children (1-17y), 'vegetable & vegetable dishes' was the key source of vitamin K_1 (26%-32%), the majority of which was attributable to 'green vegetables' (15%-16%). The contribution from fruit to vitamin K_1 intake was higher in preschool children (14%) compared to school aged children and teenagers (4-7%), partly due to the higher consumption of fruit in Irish pre-school children (113g) compared to the older age groups (80-94g). 'Potatoes & potato products' contributed 15-17% of vitamin K_1 intakes in the older age groups (5-12 y and 13-17 y), primarily due to the vitamin K_1 rich oils used in the cooking and preparation of the chips, fried and roast potatoes which contributed 12-14% of overall vitamin K_1 intakes. Similar sources of vitamin K_1 have been reported in children in the UK and US and in previous studies in Irish adults (Booth *et al.*, 1996, Duggan *et al.*, 2004, Prynne *et al.*, 2005, Hayes *et al.*, 2016).

Whilst the findings from this study suggest that current intakes of vitamin K_1 in Irish children are generally adequate to maintain normal blood coagulation, higher intakes may be required to support optimal bone growth throughout childhood. Studies in children have reported that a better vitamin K status results in improvements in bone health parameters and reduces the risk of low energy fractures (fall from the patient's own height or a fall during team games) (Kalkwarf *et al.*, 2004, O'Connor *et al.*, 2007, Van Summeren *et al.*, 2008, Popko *et al.*, 2018). Furthermore, unfavourable levels of undercarboxylated osteocalcin (measure of vitamin K status) have been identified in children throughout Europe indicating a poor vitamin K status of bone during growth (Kalkwarf *et al.*, 2004, O'Connor *et al.*, 2007, Van Summeren *et al.*, 2007, Van Summeren *et al.*, 2008, Popko *et al.*, 2018).

There are currently no data available on vitamin K_2 intakes in any population group in Ireland, partly due to limited composition data for the total and/or individual menaquinones, hence the next aim of this thesis was to estimate the intake and dietary sources of vitamin K_2 in the Irish population aged 1-90 years. As previously mentioned, the menaquinones are produced by bacteria capable of food fermentation (with the exception of MK-4) (Walther *et al.*, 2013). MK-4 is unique amongst the menaquinones and is found in foods of animal origin due to the tissue specific conversion from ingested vitamin K_1 or menadione (a synthetic form of vitamin K added to animal feed) (Okano *et al.*, 2008, Hirota *et al.*, 2013, EFSA Panel on Additives and Products or Substances used in Animal Feed, 2014). Intakes of vitamin K_2 were reported as MK-4-10 and also separately as MK-4 and MK-5-10 due to the difference in the origin and bioavailability of these menaquinones (Beulens *et al.*, 2013). Mean intakes of MK-4-10 ranged from 40-55µg/d (range across age group) in Irish children aged 1-17 years and from 42-58µg/d in adults 18-90 years. According to EFSA, there is currently insufficient knowledge available on the function, content and bioavailability of menaquinones in the body to set a dietary reference value for vitamin K_2 (EFSA Panel on Dietetic Products *et al.*, 2017).

With regard to the individual menaquinones, mean intakes of MK-4 ranged from 8-13µg/d, with 'meat & meat products' (50-67%) and 'milk' (8-25%) the key sources to intakes of MK-4 across the population groups. Mean intakes of MK-5-10 ranged from 32-45µg/d, with ‘meat & meat products’ (44-61%) and ‘cheese’ (21-37%) the key sources to intakes of MK-5-10. Of the ‘meat & meat products’, sausages accounted for between 27-51% of MK-5-10 intakes. The origin of menaquinones in sausages and other meat products is not yet fully understood, however they may be absorbed from the intestine of the animal where menaquinones are synthesized by intestinal bacteria (Fu *et al.*, 2016). MK-5-10 are produced by bacteria and their presence in foods, particularly cheese, is primarily due to the starter culture used in the fermentation process (Manoury *et al.*, 2013). To the best of this author’s knowledge, this study is the first to report vitamin K_2 intakes and dietary sources in nationally representative samples of adults and children. Prospective cohort studies have however reported the intakes of the menaquinones and their association with specific health outcomes (Geleijnse *et al.*, 2004, Nimptsch *et al.*, 2008, Gast *et al.*, 2009, Apalset *et al.*, 2010, Beulens *et al.*, 2010, Nimptsch *et al.*, 2010, Apalset *et al.*, 2011, Vissers *et al.*, 2013, Zwakenberg *et al.*, 2017). A study in the Netherlands reported intakes of MK-4 and MK-5-10 of 7 and 22µg/d respectively for the Dutch elderly (>55 years), using dietary data collected during the Rotterdam Study (Schurgers *et al.*, 1999). These intakes are lower than intakes estimated in Irish adults of a similar age.

Research has suggested that the menaquinones may play a pivotal role in reducing the risk of chronic diseases of aging, particularly the long chained menaquinones, which may protect against the development of coronary heart disease (Geleijnse *et al.*, 2004, Beulens *et al.*, 2009, Gast *et al.*, 2009). However, further research is required to fully understand the role of the menaquinones in human health including the bioavailability of the individual menaquinones.

New data on the dietary intake of Irish children aged 5-12 years have recently become available through the National Children’s Food Survey II (NCFS II) (2017-18). The final aim of this study was to estimate the intakes and dietary sources of vitamin K_1 and vitamin K_2 in Irish children aged 5-12 years from the NCFS II and to compare these data to the previous NCFS (2003-04). Similar to that described earlier for the IFCD (2012), vitamin K_1 and vitamin K_2 composition data were assigned to each food code in the NCFS II using published analytical values, recipe calculation and nutritional information on product labels. In the NCFS II database, there were no foods fortified with vitamin K_1 or vitamin K_2. However, five nutritional supplements contained vitamin K_1 (6-38µg per dose) and one nutritional supplement contained MK-7 (40µg per dose). The overall finding of this study was that there was no difference in the intake of vitamin K_1 (NCFS II: 1.4µg/kg/d, NCFS: 1.3µg/kg/d) or vitamin K_2 (NCFS II: 48µg/d, NCFS: 52µg/d) between the NCFS II (2017-18) and the previous NCFS (2003-04). The key source of vitamin K_1 in both surveys was 'vegetable & vegetable dishes' (NCFS II: 28%, NCFS: 29%), of which, green vegetables contributed 16% to vitamin K_1 intake in both surveys. Other important sources of vitamin K_1 intake in Irish children were 'meat & meat products' (NCFS II: 17%, NCFS: 11%) and 'fruit & fruit juices' (NCFS II: 12%, NCFS: 7%). 'Meat & meat products' was the key sources of MK-4 in Irish children in the NCFS II (60%) and the NCFS (59%). 'Meat & meat products' was also the key sources of MK-5-10 in Irish children accounting for 46 and 61% of intakes in the NCFS II and the NCFS, respectively. There were some slight differences in the relative contribution of individual food groups to intakes of vitamin K_1 and vitamin K_2 in the NCFS II compared to the NCFS, due to changes in dietary patterns including a higher intake of 'fresh meat & meat dishes' and fruit and a lower intake of milk and 'potatoes & potato products' in the NCFS II compared to the previous NCFS (Irish Universities Nutrition Alliance, 2019).

The present thesis has a number of strengths. The use of nationally representative high quality dietary data (including brand level detail and recipes of composite dishes) for estimating intakes and sources of vitamin K in the Irish population is a key strength of this study. The detailed methodology used to assign vitamin K values to each food consumed, which included the calculation of the vitamin K content of recipes at ingredient level is a further strength of this study. This study is also the first to report intake and sources of vitamin K_1 in nationally representative samples of children (including changes since 2003-04 in school-aged children) and intake and sources of vitamin K_2 in nationally representative samples of all age groups. Whist under reporting of energy intake is a known limitation with dietary assessment, this issue was minimised by high levels of researcher-participant interaction across each survey (three visits over the 4-day recording period for the NCFS II, NPNS and the NANS and 4 visits over the 7-day recording period for the NCFS and the NTFS).

To conclude, this study was the first to estimate the intake, adequacy and dietary sources of vitamin K_1 and vitamin K_2, in nationally representative samples of the Irish population aged 1-90 years. Vitamin K_1 intakes in Irish children aged 1-4 and 5-12 years were 2.2 and 1.3µg/kg/d, respectively, which are above the AI of 1µg/kg/d set by EFSA to maintain normal blood coagulation (EFSA Panel on Dietetic Products *et al.*, 2017). However, intakes in teenagers aged 13-17 years (0.9µg/kg/d) were below the AI. 'Vegetable & vegetable dishes' was the key source of vitamin K_1 in Irish children of all age-groups (26%-32%). For vitamin K_2, mean intakes of MK-4 and MK-5-10 ranged from 8-13µg/d and 32-45 µg/d, respectively in the Irish population aged 1-90 years however, no conclusion can be drawn on the adequacy of menaquinone intake, as there are currently no dietary reference values for vitamin K_2 (EFSA Panel on Dietetic Products *et al.*, 2017). 'Meat & meat products' was the key source of MK-4 (50-67%) and MK-5-10 (44-61%) in Irish children and adults. For school aged children, there was no difference in the intake or sources of vitamin K_1 or vitamin K_2 between the NCFS II (2017-18) and the NCFS (2003-04) despite changes in dietary patterns such as a higher intake of 'fresh meat & meat dishes' and whole fruit and a lower intake of milk and 'potatoes & potato products' in the NCFS II compared to the NCFS (Irish Universities Nutrition Alliance, 2019).

The data presented in this study will add to the small pool of data available on vitamin K_1 and vitamin K_2 intakes and sources in nationally representative samples of population groups and provides further data on the vitamin K composition of foods in Ireland.

While current intakes of vitamin K seem adequate to maintain normal blood coagulation, evidence suggests they might not be sufficient to support the carboxylation of all vitamin K dependent proteins with potential roles in bone health, cardiovascular health, cognition and anti-inflammatory functions. Food based strategies may be needed to increase intakes of vitamin K for optimum health of all population groups.

Further research should consider the need for analytical values for the vitamin K content of foods. A uniform method of reporting vitamin K composition (whether vitamin K_1, vitamin K_2 or total vitamin K) is needed to allow comparison of the vitamin K content of foods between countries. Future national dietary surveys across Europe should include vitamin K in their assessment of nutrient intakes in healthy population groups and further investigation into the bioavailability and function of the individual forms of vitamin K is required. There is also a need to establish cut off values for biomarkers of vitamin K status, which would allow dietary reference values for population groups to be determined.

References

Apalset, E., Gjesdal, C., Eide, G., W. Johansen, A.-M., Drevon, C. & Tell, G. 2010. *Dietary vitamins K1, K2 and bone mineral density: The Hordaland Health Study*.

Apalset, E., Gjesdal, C. G., Eide, G. E. & Tell, G. S. (2011). Intake of vitamin K1 and K2 and risk of hip fractures: The Hordaland Health Study. *Bone,* 49**,** 990-5.

Beulens, J. W., Booth, S. L., van den Heuvel, E. G., Stoecklin, E., Baka, A. & Vermeer, C. (2013). The role of menaquinones (vitamin K(2)) in human health. *British Journal of Nutrition,* 110**,** 1357-68.

Beulens, J. W., Bots, M. L., Atsma, F., Bartelink, M. L., Prokop, M., Geleijnse, J. M., Witteman, J. C., Grobbee, D. E. & van der Schouw, Y. T. (2009). High dietary menaquinone intake is associated with reduced coronary calcification. *Atherosclerosis,* 203**,** 489-93.

Beulens, J. W., van der, A. D., Grobbee, D. E., Sluijs, I., Spijkerman, A. M. & van der Schouw, Y. T. (2010). Dietary phylloquinone and menaquinones intakes and risk of type 2 diabetes. *Diabetes Care,* 33**,** 1699-705.

Bolton-Smith, C., Price, R. J., Fenton, S. T., Harrington, D. J. & Shearer, M. J. (2000). Compilation of a provisional UK database for the phylloquinone (vitamin K1) content of foods. *British Journal of Nutrition,* 83**,** 389-99.

Booth, S. L. (2009). Roles for vitamin K beyond coagulation. *The Annual Review of Nutrition,* 29**,** 89-110.

Booth, S. L., Pennington, J. A. & Sadowski, J. A. (1996). Food sources and dietary intakes of vitamin K-1 (phylloquinone) in the American diet: data from the FDA Total Diet Study. *Journal of the American Dietetic Association,* 96**,** 149-54.

Booth, S. L., Sadowski, J. A., Weihrauch, J. L. & Ferland, G. (1993). Vitamin K1 (Phylloquinone) Content of Foods: A Provisional Table. *Journal of Food Composition and Analysis,* 6**,** 109-120.

Damon, M., Zhang, N. Z., Haytowitz, D. B. & Booth, S. L. (2005). Phylloquinone (vitamin K1) content of vegetables. *Journal of Food Composition and Analysis,* 18**,** 751-758.

Dismore, M. L., Haytowitz, D. B., Gebhardt, S. E., Peterson, J. W. & Booth, S. L. (2003). Vitamin K content of nuts and fruits in the US diet. *Journal of the American Dietetic Association,* 103**,** 1650-2.

Duggan, P., Cashman, K. D., Flynn, A., Bolton-Smith, C. & Kiely, M. (2004). Phylloquinone (vitamin K1) intakes and food sources in 18-64-year-old Irish adults. *British Journal of Nutrition,* 92**,** 151-8.

EFSA Panel on Additives and Products or Substances used in Animal Feed (2014). Scientific Opinion on the safety and efficacy of vitamin K3 (menadione sodium bisulphite and menadione nicotinamide bisulphite) as a feed additive for all animal species. *EFSA Journal,* 12**,** 3532.

EFSA Panel on Dietetic Products, N., Allergies, Turck, D., Bresson, J.-L., Burlingame, B., Dean, T., Fairweather-Tait, S., Heinonen, M., Hirsch-Ernst, K. I., Mangelsdorf, I., McArdle, H. J., Naska, A., Nowicka, G., Pentieva, K., Sanz, Y., Siani, A., Sjödin, A., Stern, M., Tomé, D., Van Loveren, H., Vinceti, M., Willatts, P., Lamberg-Allardt, C., Przyrembel, H., Tetens, I., Dumas, C., Fabiani, L., Ioannidou, S. & Neuhäuser-Berthold, M. (2017). Dietary reference values for vitamin K. *EFSA Journal,* 15**,** e04780.

Elmadfa, I., Hasenegger, V., Wagner, K., Putz, P., Weidl, N.-M., Wottawa, D., Kuen, T., Seiringer, G., Meyer, A., Sturtzel, B., Kiefer, I., Zilberszac, A., Sgarabottolo, V., Meidlinger, B. & Rieder, A. (2012). Österreichischer Ernährungsbericht 2012.

Elmadfa, I. & Meyer, A. L. (2010). Importance of food composition data to nutrition and public health. *European Journal of Clinical Nutrition,* 64 Suppl 3**,** S4-7.

Fu, X., Shen, X., Finnan, E. G., Haytowitz, D. B. & Booth, S. L. (2016). Measurement of Multiple Vitamin K Forms in Processed and Fresh-Cut Pork Products in the U.S. Food Supply. *Journal of Agricultural and Food Chemistry,* 64**,** 4531-5.

Gast, G. C., de Roos, N. M., Sluijs, I., Bots, M. L., Beulens, J. W., Geleijnse, J. M., Witteman, J. C., Grobbee, D. E., Peeters, P. H. & van der Schouw, Y. T. (2009). A high menaquinone intake reduces the incidence of coronary heart disease. *Nutrition, Metabolism, and Cardiovascular Diseases,* 19**,** 504-10.

Geleijnse, J. M., Vermeer, C., Grobbee, D. E., Schurgers, L. J., Knapen, M. H., van der Meer, I. M., Hofman, A. & Witteman, J. C. (2004). Dietary intake of menaquinone is associated with a reduced risk of coronary heart disease: the Rotterdam Study. *Journal of Nutrition,* 134**,** 3100-5.

Halder, M., Petsophonsakul, P., Akbulut, A. C., Pavlic, A., Bohan, F., Anderson, E., Maresz, K., Kramann, R. & Schurgers, L. (2019). Vitamin K: Double Bonds beyond Coagulation Insights into Differences between Vitamin K1 and K2 in Health and Disease. *International Journal of Molecular Sciences,* 20**,** 896.

Hannon, E. M., Cashman, K., Kiely, M. & Flynn, A. (2007). Phylloquinone intakes and food sources in Irish children aged 5-12 years. *Proceedings of the Nutrition Society,* 66**,** 32A-114A.

Hayes, A., Hennessy, A., Walton, J., McNulty, B. A., Lucey, A. J., Kiely, M., Flynn, A. & Cashman, K. D. (2016). Phylloquinone Intakes and Food Sources and Vitamin K Status in a Nationally Representative Sample of Irish Adults. *Journal of Nutrition,* 146**,** 2274-2280.

Hirota, Y., Tsugawa, N., Nakagawa, K., Suhara, Y., Tanaka, K., Uchino, Y., Takeuchi, A., Sawada, N., Kamao, M., Wada, A., Okitsu, T. & Okano, T. (2013). Menadione (vitamin K3) is a catabolic product of oral phylloquinone (vitamin K1) in the intestine and a circulating precursor of tissue menaquinone-4 (vitamin K2) in rats. *Journal of Biological Chemistry,* 288**,** 33071-80.

Irish Universities Nutrition Alliance (2019). *National Children's Food Survey II: Summary report on Food and Nutrient Intakes, Body Weight, Physical Activity and Eating Behaviours in Children Aged 5-12 Years in Ireland*

Kalkwarf, H. J., Khoury, J. C., Bean, J. & Elliot, J. G. (2004). Vitamin K, bone turnover, and bone mass in girls. *American Journal of Clinical Nutrition*, 80**,** 1075-80.

Manios, Y., Grammatikaki, E., Papoutsou, S., Liarigkovinos, T., Kondaki, K. & Moschonis, G. (2008). Nutrient intakes of toddlers and preschoolers in Greece: the GENESIS study. *Journal of the American Dietetic Association*, 108**,** 357-61.

Manoury, E., Jourdon, K., Boyaval, P. & Fourcassie, P. (2013). Quantitative measurement of vitamin K2 (menaquinones) in various fermented dairy products using a reliable high-performance liquid chromatography method. *Journal of Dairy Science,* 96**,** 1335-46.

McGuire, S. (2011). U.S. Department of Agriculture and U.S. Department of Health and Human Services, Dietary Guidelines for Americans, 2010. 7th Edition, Washington, DC: U.S. Government Printing Office, January 2011. *Advances in Nutrition,* 2**,** 293-4.

Nimptsch, K., Rohrmann, S., Kaaks, R. & Linseisen, J. (2010). Dietary vitamin K intake in relation to cancer incidence and mortality: results from the Heidelberg cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC-Heidelberg). *American Journal of Clinical Nutrition,* 91**,** 1348-58.

Nimptsch, K., Rohrmann, S. & Linseisen, J. (2008). Dietary intake of vitamin K and risk of prostate cancer in the Heidelberg cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC-Heidelberg). *American Journal of Clinical Nutrition,* 87**,** 985-92.

O'Connor, E., Molgaard, C., Michaelsen, K. F., Jakobsen, J., Lamberg-Allardt, C. J. & Cashman, K. D. (2007). Serum percentage undercarboxylated osteocalcin, a sensitive measure of vitamin K status, and its relationship to bone health indices in Danish girls. *British Journal of Nutrition,* 97**,** 661-6.

Okano, T., Shimomura, Y., Yamane, M., Suhara, Y., Kamao, M., Sugiura, M. & Nakagawa, K. (2008). Conversion of phylloquinone (Vitamin K1) into menaquinone-4 (Vitamin K2) in mice: two possible routes for menaquinone-4 accumulation in cerebra of mice. *Journal of Biological Chemistry,* 283**,** 11270-9.

Popko, J., Karpinski, M., Chojnowska, S., Maresz, K., Milewski, R., Badmaev, V. & Schurgers, L. J. (2018). Decreased Levels of Circulating Carboxylated Osteocalcin in Children with Low Energy Fractures: A Pilot Study. *Nutrients,* 10.

Presse, N., Potvin, S., Bertrand, B., Calvo, M. S. & Ferland, G. (2015). Phylloquinone content of herbs, spices and seasonings. *Journal of Food Composition and Analysis,* 41**,** 15-20.

Prynne, C. J., Thane, C. W., Prentice, A. & Wadsworth, M. E. (2005). Intake and sources of phylloquinone (vitamin K(1)) in 4-year-old British children: comparison between 1950 and the 1990s. *Public Health Nutrition,* 8**,** 171-80.

Public Health England Composition of Foods Integrated Dataset. 2015. *McCance and Widdowson's The Composition of Foods Integrated Dataset 2015* [Online]. Available: https://www.gov.uk/government/publications/composition-of-foods-integrated-dataset-cofid.

Rand, W., A T Pennington, J., P Murphy, S. & Klensin, J. 1991. *Compiling data for food composition data bases*.

Schakel, S., Buzzard, I. M. & E. Gebhardt, S. 1997. *Procedures for Estimating Nutrient Values for Food Composition Databases*.

Schurgers, L. J., Geleijnse, J. M., Grobbee, D. E., Pols, H. A. P., Hofman, A., Witteman, J. C. M. & Vermeer, C. (1999). Nutritional Intake of Vitamins K1 (Phylloquinone) and K2 (Menaquinone) in The Netherlands. *Journal of Nutritional & Environmental Medicine,* 9**,** 115-122.

Schurgers, L. J. & Vermeer, C. (2000). Determination of phylloquinone and menaquinones in food. Effect of food matrix on circulating vitamin K concentrations. *Haemostasis,* 30**,** 298-307.

Shearer, M. J. & Bolton-Smith, C. (2000). The UK food data-base for vitamin K and why we need it. *Food Chemistry,* 68**,** 213-218.

Simes, D. C., Viegas, C. S. B., Araujo, N. & Marreiros, C. (2020). Vitamin K as a Diet Supplement with Impact in Human Health: Current Evidence in Age-Related Diseases. *Nutrients,* 12.

Tarvainen, M., Fabritius, M. & Yang, B. (2019). Determination of vitamin K composition of fermented food. *Food Chemistry,* 275**,** 515-522.

US Department of Agriculture (2018). Nutrient Intakes from Food and Beverages: Mean amounts consumed per Individual , by Gender and Age, What we eat in America, NHANES 2015-2016.

USDA National Nutrient Database for Standard References Release 28. 2015. Washington (DC): USDA Agricultural Research Service. Available: http://www.ars.usda.gov/nutrientdata [Accessed January 2016].

Van Summeren, M., Braam, L., Noirt, F., Kuis, W. & Vermeer, C. (2007). Pronounced elevation of undercarboxylated osteocalcin in healthy children. *Pediatric Research,* 61**,** 366-70.

Van Summeren, M. J., van Coeverden, S. C., Schurgers, L. J., Braam, L. A., Noirt, F., Uiterwaal, C. S., Kuis, W. & Vermeer, C. (2008). Vitamin K status is associated with childhood bone mineral content. *British Journal of Nutrition,* 100**,** 852-8.

Vermeer, C. & Theuwissen, E. (2011). Vitamin K, osteoporosis and degenerative diseases of ageing. *Menopause Int,* 17**,** 19-23.

Vissers, L. E., Dalmeijer, G. W., Boer, J. M., Monique Verschuren, W. M., van der Schouw, Y. T. & Beulens, J. W. (2013). Intake of dietary phylloquinone and menaquinones and risk of stroke. *J Am Heart Assoc,* 2**,** e000455.

Walther, B. & Chollet, M. (2017). Menaquinones, Bacteria, and Foods: Vitamin K2 in the Diet.

Walther, B., Karl, J. P., Booth, S. L. & Boyaval, P. (2013). Menaquinones, bacteria, and the food supply: the relevance of dairy and fermented food products to vitamin K requirements. *Advances in Nutrition,* 4**,** 463-73.

Yngve, A., Wolf, A., Poortvliet, E., Elmadfa, I., Brug, J., Ehrenblad, B., Franchini, B., Haraldsdóttir, J., Krølner, R., Maes, L., Pérez-Rodrigo, C., Sjöström, M., Thórsdóttir, I. & Klepp, K. I. (2005). Fruit and Vegetable Intake in a Sample of 11-Year-Old Children in 9 European Countries: The Pro Children Cross-Sectional Survey. *Annals of Nutrition and Metabolism,* 49**,** 236-245.

Zwakenberg, S. R., den Braver, N. R., Engelen, A. I. P., Feskens, E. J. M., Vermeer, C., Boer, J. M. A., Verschuren, W. M. M., van der Schouw, Y. T. & Beulens, J. W. J. (2017). Vitamin K intake and all-cause and cause specific mortality. *Clinical Nutrition,* 36**,** 1294-1300.

Appendix I 19 Food Groups

1. Grains, rice, pasta and savouries.

2. Bread & rolls

3. Breakfast cereals

4. Biscuits, cakes & pastries

5. Milk & yoghurt

6. Creams, ice-creams & chilled desserts

7. Cheeses

8. Butter, spreading fats & oils

9. Eggs & egg dishes

10. Potatoes & potato products

11. Veg & veg dishes

12. Fruit & fruit juices

13. Fish & fish dishes

14. Meat & meat products

15. Beverages

16. Sugars, confectionery, preserves & savoury snacks

17. Soups, sauces & miscellaneous foods

18. Nutritional supplements

19. Nuts, seeds, herbs & spices

Appendix II 77 Food Groups

1. Rice & pasta, flours, grains & starch
2. Savouries
3. White sliced bread & rolls
4. Wholemeal & brown bread & rolls
5. Other breads
6. RTEBC
7. Other breakfast cereals
8. Biscuits including crackers
9. Cakes, pastries & buns
10. Whole milk
11. Low fat, skimmed & fortified milks
12. Other milks & milk based beverages
13. Creams
14. Cheeses
15. Yoghurts
16. Ice creams
17. Desserts
18. Rice puddings & custards
19. Eggs & egg dishes
20. Butter (over 80% fat)
21. Low fat spreads (under 40% fat)
22. Other fat spreads (40%-80% fat)
23. Oils (not including those used in recipes)

24. Hard cooking fats
25. Potatoes (boiled, baked, mashed)
26. Processed & homemade potato products
27. Chipped, fried & roasted potatoes
28. Vegetable & pulse dishes
29. Peas, beans & lentils
30. Green vegetables
31. Carrots
32. Salad vegetables
33. Other vegetables
34. Tinned or jarred vegetables
35. Fruit juices & smoothies
36. Bananas
37. Other fruits
38. Citrus fruits
39. Tinned fruits
40. Nuts & seeds, herbs & spices
41. Fish & fish products
42. Fish dishes
43. Bacon & ham
44. Beef & veal
45. Lamb
46. Pork
47. Chicken, turkey & game

48. Offal & offal dishes

49. Beef & veal dishes

50. Lamb, pork & bacon dishes

51. Poultry & game dishes

52. Burgers

53. Sausages

54. Meat pies & pastries

55. Meat products

56. Alcoholic beverages

57. Sugars, syrups, preserves & sweeteners

58. Chocolate confectionery

59. Non-chocolate confectionery

60. Savoury snacks

61. Soups, sauces & miscellaneous foods

62. Nutritional supplements

63. Teas

64. Coffees

65. Other beverages

66. Carbonated beverages

67. Diet carbonated beverages

68. Squashes, cordials & fruit juice drinks

69. Infant cereals

70. Infant biscuits/rusks

71. Infant milks

72. Fromage Frais

73. Infant desserts (excluding pureed fruit)

74. Infant meals, vegetable

75. Fruit purees and smoothies

76. Infant meals, fish

77. Infant meals, meat