# Micronutrients in Long-Term Care (LTC):

# **Issues and opportunities for improvement**

by

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## **AUTHOR'S DECLARATION**

This thesis consists of material all of which I authored or co-authored: see Statement of Contributions included in the thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

## STATEMENT OF CONTRIBUTIONS

Chapter 7 was a joint effort of several co-authors. Portions of this chapter has been accepted for publication and copyright has been assigned to the Canadian Journal of Dietetic Practice and Research.

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with only the following notable exceptions: 1) increased methodological details in the thesis, 2) inclusion of 3 figures detailing how micronutrient contents of current Long-Term Care menus compared to Super-Menus in meeting the Recommended Dietary Allowance/Adequate Intakes of vitamin D, vitamin E, and potassium, and 3) a 5-day Super-Menu sample menu. The inclusion of this article as part of this thesis has been approved by the editor of the journal. This study was designed and conducted by Ivy Lam and Dr. Heather Keller. Ivy Lam performed all the data collection and analysis. Dr. Lisa Duizer and Dr. Ken Stark contributed to the formatting, review, correction, and presentation of the tables in this chapter.

Chapter 8 was also a joint effort of several co-authors. Portions of this chapter has been accepted for publication and copyright has been assigned to the Journal of Nursing Home Research:

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with the exceptions of: 1)increased methodological detail, and 2) supplementary data (e.g. recruitment letters, specific survey results) in the appendices. The inclusion of this article as part of this thesis has been approved by the editor of the journal. This study was designed and conducted by Dr. Heather Keller and Ivy Lam. Dr. Lisa Duizer, Dr. Ken Stark, and Dr. Alison Duncan formed the advisory committee to guide the creation of interview questions, and suggested potential experts for key informant interviews. Ivy Lam and Dr. Heather Keller conducted all of the webinars, key informant interviews, and in-person focus groups. Note-taking during focus groups was done by Kaylen Pfisterer.

All aspects of this thesis not listed above were authored by myself, Ivy Lam.

#### Abstract

**<u>BACKGROUND</u>**: Malnutrition is common among long-term care (LTC) residents, yet there is limited research on micronutrient (vitamin and mineral) malnutrition in the LTC setting. Micronutrient deficiencies may exacerbate symptoms of dementia, depression, infections, osteoporosis, and other prevalent conditions in LTC.

**<u>PURPOSE</u>**: This research accomplishes phase 1 of a multi-phase study, with the overall research objective of investigating the potential and extent of micronutrient malnutrition in LTC and identifying and developing food-first strategies to improve micronutrient intake in LTC residents. This was done through four sub-studies (detailed below):

**<u>METHODS & FINDINGS</u>**: Each method and respective findings/conclusions are described below.

#### Sub-Studies 1 and 2: Scoping Review Observational (SRO) and Intervention (SRI)

**Methods:** A rigorous scoping review was conducted using selected key terms in four health-related electronic databases. The initial search identified 2248 eligible titles and abstracts for screening with inclusion/exclusion criteria. **Results: SRO** (n=50 citations): Intake for vitamin D, folate, calcium, vitamin E and B6 were consistently <50% of the Recommended Dietary Allowance (RDA) regardless of divergent food intake assessment methods. More than one study found biomarkers to be low for vitamin D, C, folate, and iron in LTC residents. **SRI** (n=25 citations): Vitamin D and calcium were the most common micronutrients to be included in both pill supplementation and food fortification interventions. Different formulations (e.g. single vs. multi-nutrient) were trialed, making comparisons difficult. Supplementation and fortification demonstrated efficacy but no studies comparing these strategies were identified. **Conclusion:** Findings suggest that micronutrient intake and biochemical status are suboptimal for key nutrients in LTC. Single nutrient interventions predominated and more work on efficacy of multi-nutrient physiological doses, whether in supplemental or fortification formulations is needed. Limited fortification studies have been completed and there is a need to determine efficacy for prevention as compared to supplementation. More research on fortification doses and formulations that are acceptable and efficacious is also required.

<u>Menu Analysis (MA) and Super-Menus (SM)</u> Methods: Regular, non-therapeutic menus (week 1, all meals) from diverse LTC homes (n=5) across Canada were analyzed for micronutrient content using Food Processor with the Canadian Nutrient File. EaTracker was used to determine Canada's Food Guide servings. Site dietitians provided home recipes/portion sizes, and validated menu analyses. SM were designed to meet micronutrient needs without increasing volume and calories, considering the preferences and portion sizes used in LTC. **Results:** Despite planning to and generally meeting CFG recommendations, menus' nutrient content varied significantly across homes. Micronutrients of greatest concern across all menus were vitamins D ( $8.90 \pm 5.29 \mu g/d$ ) and E ( $5.13 \pm 1.74 mg/d$ ). Folate,

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magnesium, and potassium were also below recommended values. SM were significantly higher in several nutrients as compared to home menus, but still were unable to meet vitamin D ( $11.2 \pm 2.54 \mu g$ , mean 56% RDA), E ( $12.6 \pm 4.08$ , 84% RDA) and potassium ( $4018 \pm 489 \text{ mg}$ , 85%) recommendations. **Conclusion:** Evidently, current guidelines for menu planning may be inadequate to address micronutrient needs, and more nutrient-dense strategies need to be explored in LTC. Careful menu planning results in most micronutrients recommendations being met.

Acceptability Testing (AT) Prior to implementation, potential interventions should be assessed for their need, feasibility, and acceptability with knowledge users. Methods: Online LTC Staff webinar focus groups, expert Key Informant interviews and in-person focus groups (residents and family) were conducted to develop and determine the acceptability of a micronutrient fortification strategy. Polling and rating questions provided quantitative data to confirm qualitative data. **Results:** Focus groups and key informant interviews provided insight into potential food vehicles for fortification (e.g. soups, desserts, condiments), production and regulatory issues, and helped to develop the strategy to minimize anticipated barriers and promote uptake. Development of outsourced/pre-made fortified products was the preferred intervention, with mandatory training and clear protocols for preparers to ensure appropriate use. **Conclusion:** Knowledge users can envision food fortification as a potential intervention if products are easy to access and incorporate into current production systems. All stakeholders desire efficacy research to support use of this strategy in LTC.

**OVERALL:** Triangulation of methods (SRI, SRO, MA/SM, and AT) and findings offers a multidimensional understanding of potential micronutrient deficiencies in LTC and food-first strategies that can be used to prevent this form of malnutrition. In general, food-first interventions in LTC to prevent or ameliorate micronutrient deficiency are lacking and quality menu planning using the DRI as a guide and food fortification are plausible strategies. Further work is needed to determine the relationship between micronutrient intake and biomarkers of function; does sufficient micronutrient nutrition support the overall health and quality of life of residents. Greater knowledge and awareness of micronutrient qualities of foods and of best practices in food-preparation methods through better training and education of LTC health providers is needed to ensure uptake. This work provides foundation for a micronutrient food fortification strategy to address malnutrition in LTC.

#### Acknowledgements

"Teach us to number our days, that we may gain a heart of wisdom." Psalm 90:12

We know so little about how our choices might influence our paths. I would, then, like to dedicate this work to those who have influenced my choices: To Mum and Dad, for teaching me to respect my elders and setting an example in loving and caring for our elders. To my Family, much love and thanks.

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## List of Abbreviations

AMA	American Medical Association
CDC	Centers for Disease Control and Prevention
CFG	Canada's Food Guide
DRI	Dietary Reference Intakes
EAR	Estimated Average Requirement
EFR	Estimated Food Record
KI	Key Informant
ONS	Oral Nutritional Supplement
RD	Registered Dietitian
RDA	Recommended Dietary Allowance
LTC	Long-Term Care
NM	Nutrition Manager
WFR	Weighed Food Record

#### Chapter 1

#### Introduction

The number Canadians aged 65 and above living in health care institutions, including Long-Term Care (LTC) Homes is projected to double, with an anticipated 750, 000 Canadians living in these settings by 2036 (1). A similar trend is seen globally (2,3), although different formats and styles of care are available (4). While estimates of malnutrition in LTC are elusive, it is estimated to occur in 20-60% of residents in Canada (5-9); similar rates of malnutrition are seen worldwide (10–12). Adequate intake of a varied diet is needed to meet micronutrient requirements, although physiological factors including challenges with self-feeding, early satiation, taste changes, dysphagia, and decreased appetite are significant contributors to older adults' food intake, rendering them nutritionally vulnerable (13,14). Micronutrient (specifically, vitamin and mineral) status is critical to managing common health issues in LTC, including anemia, bone health (15), cognitive and functional status (16), immunity (17), infections, and wound healing (18). Micronutrient deficiency is potentially a prevalent yet preventable form of malnutrition among older adults living in long-term care (LTC) (5,19–21). These deficiencies may further aggravate poor health and low intake, leading to a vicious cycle of malnutrition and decreased function, directly impacting residents' quality of life (22).

Poor food intake is common in LTC (5,21,23). Plate waste estimation suggested that approximately 1600 kilocalories is consumed (14), with even lower consumption by cognitively impaired residents (~1,100 to 1,200 kcal per day) (5). Yet, most studies to date that rigorously collected food intake data are based on a single convenience sample, which doesn't necessarily represent the population of older adults in LTC. To further understand if micronutrients are a potential problem, rigorous review of the extant literature to summarize findings and identify research gaps is needed. Recent research has also demonstrated that menus may not provide adequate micronutrients to meet dietary recommendations, even when meals are completely consumed (5,19,24,25). Clearly, a shift towards prevention of micronutrient malnutrition is needed for this vulnerable population.

At present, there is no consensus on the best way to prevent or treat micronutrient malnutrition in LTC residents (26). In view of residents' average low food intake (5,27) and the recommended micronutrient levels to achieve nutritional adequacy (5,28), micronutrient fortification of key foods is a potential prevention method (29). Little is known about fortification and how this strategy can be developed to be useful for prevention for the majority of older adults living in care environments. Other strategies, such as micronutrient supplementation, which is typically used to treat known or suspected deficiency, may also be beneficial, but a better understanding of these strategies (including micronutrient content and dosages trialed) is needed. To move forward, agreement on the micronutrients of concern (i.e. micronutrients that residents are at highest risk of deficiencies for), based on poor intake or biochemical status is needed for the LTC sector. Moreover, identifying stakeholders' perspectives of micronutrient fortification will enhance understanding of both the practicality and potential barriers to implementation of this strategy. This thesis will begin to bridge these gaps to support micronutrient nutrition of older adults living in LTC.

#### Chapter 2

#### Background

#### 2.1 Overview of Assessing Nutritional Status and Limits of this Thesis

Nutritional status of residents living in LTC is measured comprehensively by using several methods, including: clinical characteristics (e.g. factors that place an individual at risk of poor intake such as requiring eating assistance), environmental factors impacting food intake (e.g. micronutrient content of menus), body size and composition (e.g. weight for height), food intake (i.e. dietary status), functional parameters (e.g. strength, capacity for activities) and biochemical markers of nutritional state (i.e. serum albumin, micronutrient-related biomarkers) (30,31). To determine micronutrient status specifically, three measures are commonly used: food intake, biochemical markers of the micronutrient and functional outcomes of adequate/inadequate status (e.g. vitamin D and fractures) (31,32). Intake has to be adequate to meet individual requirements for biochemical markers to be at a normal level, which then influences body and tissue functions that require the nutrient. Research may undertake only one or two of these assessment areas in an attempt to understand micronutrient status, but true status can only be determined from functional markers (32,33). This thesis will be focused on the two former methods and a review of terminology, concepts and methods will be first provided. A brief literature of micronutrient food intake and biochemical status will then be outlined.

#### 2.2 Diet Assessment Terminology & Methodology

#### 2.2.1 Terminology: Dietary Reference Intakes

The Dietary Reference Intakes (DRIs) were developed by the Institute of Medicine (IOM) of The National Academies in order to provide reference values of nutrients for which to guide nutrition intake or assess and plan diets for **healthy** populations in the United States and Canada (33). Specific values are given for different age groups, gender, and life stage (34). Other dietary references have been developed around the world (35), but this thesis will focus on the DRIs as set by the IOM. Within the DRIs are several terms and concepts which will be addressed below.

RDA: The Recommended Dietary Allowance (RDA) provides a reference for meeting nutrient requirements for nearly all (97-98%) healthy individuals in a particular gender, age, and life stage group (e.g. those >70 years old) (28). This is the goal to which individuals would target their intake, as an individual's requirements are typically unknown (36). The RDA is set where there is an established Estimated Average Requirement (EAR). Understandably, certain individuals may require nutrient levels higher than the RDA, but the RDA covers the needs of the majority.

EAR: The Estimated Average Requirement (EAR) is the level of average daily nutrient intake estimated to meet half (50%) of the population's requirements, based on their given age and gender group. These levels have been established based on a thorough literature review identifying requirements for a population group based on use of functional markers of status (33). In general, the RDA is calculated from the EAR using this equation: RDA = EAR + 2 SD, where the RDA is the EAR plus two times its standard deviation (SD).

AI: Adequate Intake (AI) is used in the place of the RDA if an EAR (thus, RDA) has not been established for a particular micronutrient due to insufficient scientific data (34). The AI is developed from observed or experimental estimates of the nutrient intake of groups of healthy individuals who are assumed to have adequate intake (34). For instance, since EARs have not been developed for vitamin K, pantothenic acid, biotin, choline, chromium, fluoride, manganese, these micronutrients will have an AI instead.

UL: The Tolerable Upper Intake Levels (UL) is used to determine the highest level of long-term daily intake for individuals that does not present adverse health effects (28,37). Logically, should intake increase above the UL, the risk of adverse effects would also increase (28). The UL is useful in areas of food fortification or supplementation, as the UL typically takes into account the total intake of nutrient from natural food, fortified food, or supplements (34). Those at higher risk of toxicity would be those who consume a large amount of key foods, select a higher proportion of fortified foods, or who take supplements as well as fortified foods (37). Certain nutrients are not presented with a UL due to insufficient data, not because there are no adverse effects from high intakes of these nutrients; it is recommended that extra caution be given when consuming high amounts of these nutrients (34).

#### 2.2.2 Methods: Dietary Intake Assessment

Dietary assessment is a less invasive method of assessing nutrient or nutritional status compared to physiological methods, and can be used as an initial measurement of potential inadequate or excess intake, to be then be paired with physiological and/or biochemical measures for a more accurate assessment (30). Dietary assessments include retrospective methods (e.g. Food Frequency Questionnaires (FFQ), dietary surveys, 24-hour recalls, diet histories) and prospective methods (e.g. estimated food records (EFR), weighed food records (WFR), and duplicate portion analysis) (31). While other dietary assessment methods exist, only those encountered in the conduct of this thesis will be explained. Description of methods have been focused for the LTC context.

#### **Retrospective Methods**

24-hour recall: Participants report on past food and beverage consumption for a 24-hour timeframe, with a trained interviewer probing on portion size, frequency, and missed items (31).

Although potentially useful in some LTC environments, potentially with the respondent being staff, this method is not commonly used due to limits of memory and recall of residents.

Food Frequency Questionnaire (FFQ): Participants are provided a list of foods in different categories (e.g. by food group) consumed over a specified period (e.g. past month, past year) to select from. This can be done individually, or administered by a staff or the researcher. FFQs may be tailored to a specific nursing home diet/menus, but are also limited by the memory of residents.

*Diet history:* Participants report on all food and beverages consumed over a usual day or number of days to a trained interviewer, who will also probe on portion size, frequency, and missed items (31). This can be combined with food diaries to help participants to recall and increase accuracy of the report.

#### **Prospective Methods**

*Weighed food record (WFR):* Trained staff or researcher weighs foods (either entire plate, or separately weighing components of food on the plate) on a scale before it is served to the participant. A reference plate's weight may also be used as a standard pre-serving weight. Leftovers are reweighed, and the weight difference before and after the meal is calculated and recorded.

*Estimated Food Record (EFR):* Trained staff or researcher observes participants' intake at mealtimes (and snack-time) and records the amount of foods consumed. This can be recorded in terms of range of percentage of the food consumed (e.g. 50-75% consumed).

*Food Diary:* The participants record all food and beverages consumed in household measures (by estimate or actual measures), usually over a number of days (31). This may be done by staff as capacity of residents to complete the diary may be limited.

*Duplicate Portion Analysis:* A researcher or trained staff weighs or measures a duplicate identical portion of food and beverages consumed by the participant.

Retrospective methods are considered inferior to prospective methods as they rely on recall of the participant and items can be missed; thus they are less accurate (38). Although prospective methods measure 'actual' intake as intake is recorded as consumed, no method adequately represents true intake of an individual, as prospective methods are known to change eating behavior (31). How close the dietary assessment represents 'true diet' is also influenced by the number of days of diet collection. Yet, different numbers of days of collection are needed to represent usual intake, depending on the nutrients assessed (30). Certain procedures within an assessment method may also be more accurate than others (e.g. weighed food records vs. estimated food records). Consideration of administration time and participant burden impact the choice of dietary assessment method and need to be balanced against need for representativeness and accuracy of intake (31). Thus, the reality is that few to no individual food intake studies will be of sufficient rigor to fully address the question of which micronutrients are inadequately consumed in LTC residents. A rigorous review of the literature to date could provide a basis for this understanding.

#### 2.2.3 Biochemical Assessment of Micronutrients

In addition to dietary intake, biomarkers or biochemical measurements of micronutrients provide a snapshot of their levels or their activity in the body (e.g. PTH for vitamin D and calcium status) (39). Biomarkers may be a more accurate method to determine potential micronutrient deficiency for some nutrients, due to absorption, storage and utilization differences among individuals (39,40). For better accuracy, several studies have examined both dietary intake and biochemical data, finding that intake assessment may identify inadequate micronutrient intake, but micronutrient biomarker statuses may still be within normal limits (20,41–43). A review that rigorously accumulates this evidence to determine those micronutrients that may be inadequate for residents living in in LTC, based on an assessment of biomarker status in addition to dietary intake is needed.

When conducting research on micronutrient status, individual laboratories conducting biochemistry and researchers in their won labs often use their own cut-offs to determine potential inadequacy of a nutrient. To be able to compare citations, a common reference is needed. Reference ranges for what is considered normal is available for most nutrients from the American Medical Association (AMA); these 'normal' ranges are used in both scientific and medical settings (44). The Centers for Disease Control and Prevention (CDC) also provides reference cut-offs for values that are below normal, at low and/or deficient values (45).

Additional limitations with biochemistry assessments include issues with sensitivity and reliability of existing biomarkers, where some have limited usefulness due to tight self-regulation (e.g. serum calcium) or lack in sensitivity (e.g. decreases do not always indicate deficient states) or specificity (changes in response to more than one micronutrient status) (39,46). Potential biomarkers for assessing micronutrient status are under development (40,47). All of these add to the challenge in identifying micronutrients that are potentially inadequate.

#### 2.3 Food Intake in Long-Term Care & the Potential for Micronutrient Inadequacy

Malnutrition in LTC has been well-documented, affecting 20-60% of residents (5–9). Low food intake in LTC has been measured in practice and research (5,24,48). Micronutrient deficiency (specifically, vitamin and mineral) is a potentially prevalent yet preventable form of malnutrition among older adults living in LTC (5,19–21). Moreover, micronutrient status is critical to managing common health issues in LTC, including anemia, bone health (15), cognitive and functional status (16), immunity (17), infections, and wound healing (18). Deficiencies may further aggravate poor health and low intake, leading to a vicious cycle of malnutrition and decreased function, directly impacting residents' quality of life (22). Contributors to inadequate food intake include poor dentition (49), declining health requiring modified texture diets (50), and other disease states requiring higher nutrient needs (12). One study measured plate waste and found that residents, on average, consumed about 1600 kcal/day (14). Intake may be lower for those with cognitive impairments, where a mean intake of 1,100 to 1,200 kcal/day has been identified (5).

To date our understanding of potentially inadequate micronutrient intake and biochemical status of nutrients is fragmented. In practice, estimated food records are commonly used to assess residents' food intake over time (51). Issues with this method include inaccuracies in reporting by nursing staff where residents' food intake is often overestimated (52,53). Additionally, records generally do not specify which portion of the meal was not consumed, lacking the specificity to assess residents' micronutrient intake, making it difficult to determine if residents are at risk of micronutrient deficiencies. In research, a variety of assessment methods have been used, from food frequency questionnaires (54) to duplicate portion analysis (55). Due to the variability in the quality of dietary assessment methods, different micronutrients are often identified to be poorly consumed creating a challenge in identifying whether micronutrient intake is actually poor in LTC, and which micronutrients are likely to be at a high risk of deficiency (41,56,57). Furthermore, studies are generally based on a single convenience sample (Viveky et al., 2012; Wakimoto & Block, 2001; Woods et al., 2009) which is not generalizable. A comprehensive review that brings together the available literature, and identifies effects seen and strategies used to address potential micronutrient inadequacies across different regions is needed

to provide some clarity to this issue. As it is unknown at this point the extent of literature focused on micronutrients in LTC, a scoping review methodology will be used to summarize the disparate data on micronutrient food intake in LTC to better understand not only consistent micronutrients that are low in the diet, but also gaps in literature.

#### 2.3.1 Physiological factors contribute to low food intake

With age comes physiological changes, including declining abilities of organ systems and impaired homeostatic regulations (60). Common physiological challenges include issues with self-feeding, early satiation, taste changes, dysphagia, and decreased appetite which often hinder older adults' food intake or affect their ability to eat, rendering them nutritionally vulnerable (13,14). Dentition (49,61) and impaired swallowing mechanisms (62–64) further limit residents' ability for adequate food and subsequently, micronutrient, consumption. As aforementioned, low food intake is prevalent in LTC. This is beyond caloric intake alone, as dietary diversification, or an adequate intake of a varied diet is also needed to meet micronutrient requirements. However, decreased physical mobility and energy expenditure may lead to decreased appetite (60), despite similar or even increased nutrient requirements (65).

Prolonged inadequate intake of micronutrients may accelerate degenerative chronic diseases such as cardiovascular disease, cognitive decline (66), and other conditions that plague the LTC population. Impaired adaptive mechanisms to oxidative stress from deficient intakes of anti-oxidative micronutrient (e.g. vitamin C, E), along with selenium and zinc, further contribute to age-related oxidative diseases (67). Thus, a vicious micronutrient malnutrition cycle is seen where physiological factors impair consumption of micronutrients, and inadequate micronutrients further aggravate disease states in residents living in LTC.

#### 2.3.2 Menu Planning and Canada's Food Guide

In addition to the physiological and psychosocial barriers to food intake in LTC that need to be considered when identifying potential micronutrient inadequacy, the menus themselves used in LTC for provision of food are another potential barrier to nutrient intake. In Canadian LTC homes, menus are currently planned with *Canada's Food Guide to Healthy Eating* (CFG) to ensure variety (55). However, CFG may be inadequate in addressing micronutrient needs in menu planning, as foods were not grouped into food groups based on nutrient content, but rather how food is traditionally consumed (5,68). Consequently, micronutrient of CFG choices differ greatly from choices within the same food group, and even the most nutrient dense food choices may still be inadequate to meet micronutrient recommendations. For instance, legumes are grouped with meats because they are used as a meat substitute, yet the micronutrient profile of legumes are much different from meat products.

Dietary Reference Intakes (DRIs) provide micronutrient recommendations, yet planning based on this reference requires knowledge of intake distribution (69), which is currently lacking in LTC. Thus, menu planners use their professional judgment with the assumption that, by following CFG and serving a variety of foods, the DRIs will be met (5). Although menus are planned to meet 100% of residents' needs, some residents may not meet their micronutrient requirement due to low food intake (5). Canadian research examining the adequacies of LTC menus using the CFG have demonstrated some improvements in nutrient provision with the 2007 revision to the guide (48), yet difficulties in meeting all micronutrient requirements with current menus continue to call for new menu planning strategies (5,70). Moreover, these studies generally examine single menus from one location, and are not generalizable. A study examining several Homes under different management from several locations in Canada may provide a more comprehensive report of the state of micronutrient provision in menu planning in LTC and

if current planning is inadequate to meet the DRI. As well to date, there has been no comparison of menus designed to meet the DRI to those based on CFG.

#### 2.4 On Food Fortification

Increasing nutrient-density of traditional foods is a way of increasing micronutrient intake and status. Historically, micronutrients and food fortification has been used to combat population-specific diseases, maintain health, and prevent illnesses worldwide (71). From iodine in salt (72,73) to folic acid and iron in cereal grains (74–77), issues like gout, spina bifida, and iron-deficiency anemia have become more rare in populations that have implemented fortification for these nutrients. Furthermore, fortification can be incorporated into staple foods, thus minimizing change and burden for consumers (71). Cost-wise, micronutrient fortification has been shown to be a cost-effective preventative method in reducing nutrient-based diseases when comparing cost of fortification to costs attributed to deficiency or hospitalization (78,79).

It is recognized that fortification will not meet all population requirements (79). Thus, guidelines to assess whether food fortification should be considered have been established (79,80). This includes the need for: an appropriate food vehicle that is consumed by the population at risk, centralized food-processing systems, evidence of prevalent deficiencies in the population, or the cost of deficiency is high even if the effects only pertain to a small group (79,80).

The majority of fortification work has targeted developing countries (Rosalind S. Gibson & Hotz, 2007; UNICEF, 2005; Usfar et al., 2009; Van der Merwe, Kluyts, Bowley, & Marais, 2007), usually targeting youth (84) and pregnant women (73). In developed countries, research on fortification target similar populations: pregnant women (85) and children (86).

However, a rapidly growing at risk population in developed countries has been overlooked– older adults in LTC. Studies have evaluated the benefits of fortification for older adults, focused on vitamin B12 and homocysteine-related cardiovascular disease (74), and vitamin D/calcium and bone diseases (87,88). This population potentially meets the criteria stated by Horton et al. (2006). However, identification of appropriate food vehicles and a structured examination of the prevalence of micronutrient deficiencies in LTC residents is required. The sections below will explain fortification regulations from both general and Canadian-specific viewpoints, and how fortification may be applied in the LTC setting.

#### 2.4.1 Food Fortification Regulations

Fortification of micronutrients (vitamin and minerals) is a strategy to maintain and/or promote nutrition in food, along with potential protection from nutrient deficiencies (89). Fortification regulations are in place to avoid excessive nutrient provision, and to ensure that adequate and consistent amounts of nutrients are added to fortified foods. Each nation has its own food fortification regulations (37,87,90).

The Codex Alimentarius Commission (the Codex), developed by the United Nations and the World Health Organization, has established general principles for adding essential nutrients into food (91). According to the Codex, essential nutrients are substances in food that cannot be made in the body, or cannot be made in adequate amounts, and these substances are needed for maintenance of health and/or growth (91). Fortification is the term used when essential nutrient(s) are added to a food that may or may not originally be in the food, with the goal of preventing or correcting potential nutrient deficiencies for a specific population (91). This is different from *restoration*, which is the addition of essential nutrients that were originally in a food but removed due to losses from the manufacturing, storage, or handling process; the purpose is to restore the original amount present prior to processing (91,92). *Standardisation* is

the term used when nutrients are added back to foods to offset natural or seasonal fluctuations in nutrient content (71).

The food vehicle is the food in which these essential nutrients will be placed. It should also be a food that is commonly consumed by the population of interest (91). The nutrient and dosage added in the fortification formulation will be based on the nutritional issues and food consumption patterns of the population of interest. The dosage of nutrient(s) added to the food should be adequate to prevent or correct the deficiency of interest based on normal consumption of the fortified food by the targeted population group, yet not high enough to lead to excessive nutrient intake by those who have high intakes of the fortified food (91). "Demonstrated need" refers to evidence of actual clinical or subclinical deficiencies, estimated risk due to low levels of nutrient intake, or potential deficiencies due to changes in food habits (91).

## **Discretionary Fortification and the Canadian Food Inspection Agency**

Canada's fortification policies presents an example of regulations around micronutrient (vitamin and mineral) fortification. The Canadian Food Inspection Agency has proposed regulations for discretionary fortification (beyond mandatory fortification, where manufacturers can choose to add additional micronutrients to foods), based on the types of micronutrients chosen for fortification (89). Three risk categories exist to group the nutrients and levels permitted for fortification:

• **Risk A nutrients:** Thiamine, riboflavin, niacin, vitamin B6, vitamin B12, pantothenate, biotin, vitamin E, vitamin C, and beta-carotene.

These are nutrients with a wide margin of safety with the Tolerable Upper Limit of Intake

(UL), nutrients with no UL set, or nutrients with narrow UL margin but has "non-serious critical adverse effects." The total percent daily value (% DV, total of naturally occurring and added) of these nutrients can be up to 20%, to make the fortified food an "excellent source" of the nutrient(s) (89)

- Risk B nutrients: Vitamin D, folate, potassium, calcium, magnesium.
   These are nutrients with serious adverse effects if taken at excessive levels, but risk of excessive intake at the proposed level of discretionary fortification is low. These nutrients can be added up to 10% DV to a food (total of naturally occurring and added) (89)
- Risk C nutrients: Nutrients not permitted in discretionary fortification: Vitamin A, zinc, iron, copper, selenium, manganese, iodine, and fluoride.
   These are nutrients that have a narrow margin of safety with serious adverse effects, and/or current intake of the population is already above the UL (89)

#### 2.4.2 Meeting Micronutrient Needs in LTC

In addition to menu planning that meets the DRI, there are two other approaches that have been used to improve micronutrient intake in LTC residents. Supplementation of micronutrients in LTC has been shown to improve bone markers and bone mass for those with vitamin D deficiencies (93,94) and ameliorate status of other micronutrients (95,96). However, contradictory results have been reported when functional outcomes were measured, where micronutrient supplementation was not shown to reduce respiratory infections (97,98), fracture rates (99), or healing times of pressure ulcers (100). There are also concerns with supplementation, including food-drug interactions (101), polypharmacy (102–104), the need for staff administration and resident compliance (105), and toxicity at high dosages (106).

Enriched/fortified foods have been proposed as a 'food first' approach to addressing nutritional issues and improving health status, requiring no change in behaviour on the part of the resident (107,108). High protein and energy ingredients (e.g. milk, eggs, or cheese) have been added to foods and shown to improve macronutrient intake (109), but these enhanced foods typically do not focus on improving micronutrient intake (107). Liquid or powdered protein supplements are also available to be added to the diet (108).

Fortification has been considered a potential solution to micronutrient malnutrition in the elderly population (29,110). Yet, few studies have examined micronutrient deficiencies and/or fortification, with the most commonly studied nutrients being vitamin D (111–114), calcium (114,115), and folate (116,117). These fortification studies have found improvements in blood vitamin levels from micronutrient fortification (29,118,119). Although not all biomarkers improve (119), one study showed no improvement in a functional score for community-dwelling older adults consuming vitamin and mineral enriched foods (120). Difficulties with fortification have been noted, such as altered taste of the enhanced food (119). However, the lack of consistency between dosage used, micronutrient added, food vehicles, and settings (community, LTC) between studies make comparisons difficult. It is also unclear how efficacious fortification is in contrast to other strategies. A comprehensive review that identifies diverse supplementation and fortification studies in LTC may provide further insight to these questions.

In view of LTC residents' average food intake levels in comparison with the micronutrient levels needed to achieve nutritional adequacy, micronutrient fortification of foods holds promise as a means of increasing nutrients without calories (19,26) and replacing supplementation which is not a preventative strategy. However, before a new intervention is

fully implemented, it is important to determine if it is acceptable and feasible to the end users (knowledge users, in our case). To date, there is minimal understanding of how acceptable food fortification would be to all stakeholders, including residents and staff.

#### 2.5 Acceptability Testing of an Intervention

Assessment of acceptability and feasibility of new interventions with knowledge and end users have been recommended to promote understanding, participation, adherence and positive outcomes of interventions, and to ensure that these approaches are applicable to the users' daily lives (121). Acceptability and feasibility are commonly confused and their definitions should be clarified. 'Acceptability' is defined as the "suitability or favorability" of an intervention, and 'feasibility' is the "ease or convenience of execution" (121–123). Both of these terms affect the researchers and the participants, yet it has been argued that 'feasibility' pertains more to the interventions' recipients and the providers/health professionals who will carry out the intervention (122). Thus, this thesis used the term 'acceptability testing' when describing participants' perception of a micronutrient fortification strategy in LTC.

Acceptability testing has been suggested to be done with end users prior to implementation, especially when the strategy requires changes in care processes (121). Involvement of stakeholders (e.g. practitioners and consumers) may enhance relevance and use of research in practice (121,124,125). Resident and family members' perspectives have also been found to be helpful in designing new programs in LTC (126). Establishment of acceptability is essential in the early stages of the intervention, prior to full implementation, to determine whether it is the lack of acceptability to the intervention (e.g. poor intervention uptake) that led to poor results, rather than failure of the intervention, per se (127).

Determining the acceptability of micronutrient fortification with stakeholders who are closely aligned with planning, purchasing, preparing and serving food (dietitians, nutrition managers, cooks), as well as with end users of food fortification (residents) and family members will enhance understanding of barriers to implementation of a potential food fortification strategy. To date there is no known acceptability testing for fortification in LTC.

#### 2.6 Triangulation of Data to Answer Research Questions

Strategies to collect diverse data to address complex issues and questions in health research have been proposed (128). Research of LTC environment and teams have generally been qualitative studies (129,130). However, researchers have expressed the need for multi-approach/methods studies to address multifaceted questions affecting care practices in LTC (131,132). Care for aged residents with complex health concerns involves many stakeholders (i.e. staff, family, and residents), and is thus an ideal context for use of diverse data collection methods and approaches, including flexibility in methodology to capture each stakeholder groups' perspectives (133). Moreover, a better understanding of the context through participants' perspectives can challenge researchers' assumptions and interpretations, providing additional critical analysis and feedback on the study and enhancing the credibility of the findings (134).

Mixed methods research that uses both quantitative and qualitative approaches in combination may provide a better understanding of research problems than a single approach alone (134). The use of surveys (quantitative) and focus groups (qualitative) has complementary strengths and supports a mix of open and closed ended questions. The combination of quantitative and qualitative methods and interpretation of findings in light of each other's results is called triangulation. Triangulation through the use, congruence, and confirmation of multiple sources of evidence helps to strengthen research validity (134). As well, where one method

informs the other, leading to new directions of research and lines of questioning, the overall quality of a study will be enhanced (134,135).

Specific to this work, the overarching research question is multifaceted and requires several angles or studies to be fully addressed. Learning and building on results from each study in a stepwise approach will result in triangulation of findings. Additionally, acceptability testing for a strategy to improve micronutrient intake in LTC requires the multiple perspectives and their triangulation of knowledge users to enhance our understanding of the acceptability of this strategy (136). Thus data within this specific study will also be triangulated.

#### 2.7 Summary of Background

In summary, poor overall intake due to physiological changes with age impacts food and micronutrient intake of residents in LTC; menu planning which is based on CFG, may be part of this problem. Yet, due to variability in diet assessment and biochemical markers and their cut-offs, often in single, convenience samples, it is still unclear if and which micronutrients are potentially inadequate in this population. A thorough review of research to date on the topic to examine results of diverse assessment methods and strategies trialed is needed to not only summarize work to date, but also identify gaps for future research. Interventions to improve micronutrient status in LTC need to be similarly summarized. Fortification is believed to be a viable strategy, but as it requires changes in practice and is a more novel approach, input from stakeholders (residents, family, health providers, experts) through acceptability testing is needed before this strategy is further formalized. Triangulation of findings from diverse perspectives and approaches is needed to address the overarching research question of if micronutrient status is a problem in LTC and how it can be improved.

#### Chapter 3

#### **Rationale and Research Questions**

#### 3.1 Rationale

While researchers agree that micronutrient inadequacies are of concern for older adults (42,137–139), the prevalence of micronutrient malnutrition in LTC is still not fully understood, and studies have not examined the full range of micronutrients that may be low for LTC residents. Moreover, the variety of strategies trialed to improve residents' micronutrient intake have yet to be documented. Thus, this thesis aims to begin to address this gap in knowledge.

#### 3.2 Research Objective and Questions

The overarching research objectives were to 1) investigate the potential and extent of micronutrient malnutrition in LTC and 2) identify and develop food-first strategies to improve micronutrient intake in LTC residents.

#### The specific research questions were:

(1) What is the range of micronutrient intake and status (biomarkers) in LTC from the literature, and how do these values compare to standard references (DRI and biomarker cut-offs) to determine the potential for micronutrient malnutrition?
Hypothesis 1: Micronutrient malnutrition (including specific micronutrient deficiencies and/or decreased intake (140)) exists in LTC and can be evidenced by assessing micronutrient intake and biomarker statuses.

(2) What feasible and effective non-oral nutritional supplement interventions for improving micronutrient status have been shown to be effective in LTC residents? *Hypothesis 2: Identified micronutrient food fortification interventions will improve micronutrient biomarker levels for LTC residents.* 

(3) What is the adequacy of micronutrient provision in LTC menus when compared to the DRI? Can a food-first menu planning strategy provide sufficient nutrients to meet residents' requirements?

*Hypothesis 3: LTC menus show variability and do not meet the RDA for several nutrients.* 

(4) Is a food fortification strategy considered acceptable by various stakeholder groups?What provisions are necessary to enhance acceptability?

*Hypothesis 4: Micronutrient fortification is an acceptable intervention for stakeholders, and be preferred over pill-forms for supporting micronutrient intake.* 

Both quantitative and qualitative methods in four linked sub-studies were used to meet research objectives. It is anticipated that a better understanding of the extent of micronutrient malnutrition in LTC and the effects of strategies trialed will inform future micronutrient-enhancing strategies, such as micronutrient food fortification. Methods and results were triangulated to provide a more comprehensive understanding to address the overarching research question.

#### Chapter 4

#### Methodological Overview

#### 4.1 Introduction to Methods

Several different methods were chosen to address the overall research question. Specifically, for Objective 1: to identify if this is an issue with respect to consumption of specific nutrients in LTC residents, a scoping review of observational studies related to LTC was undertaken. Similarly to address Objective 2, a scoping review of intervention studies of nonoral nutritional supplement (ONS) studies trialing either vitamin/mineral pills or food fortification was completed. For Objective 3, a nutrient analysis on five, 7-day LTC menus from 4 provinces was performed, and a five-day micronutrient-dense food-based super-menu was created and compared to standards, as well as these five homes. Objective 4 was focused on determining the acceptability of a micronutrient fortification strategy for LTC. To address this objective, webinar focus groups (with LTC staff), key informant interviews (with relevant experts), and in-person focus groups (with LTC residents/family) were conducted. An overview of key points in the methods to address each of these objectives is outlined below. Not every aspect of methods undertaken will be covered; rather key methodological points, will provide an overview justifying the choice of method, and demonstrate particular strengths and limitations as well as methodological processes to enhance rigor.

# 4.2 Scoping Review Methodology

A thorough literature review is needed to provide an understanding of the micronutrient needs of older adults in LTC and what interventions, outside of oral nutritional supplementation such as micronutrient fortification, have been shown to be efficacious to improve status. A scoping review was the chosen method for this literature review. This method provides an

opportunity to quickly explore a body of literature, allows for summary and dissemination of research findings, and helps identify research gaps in existing literature when the research conducted to date in a specific area is diverse (124). Scoping reviews have been recommended for areas of research that have yet to be reviewed in a thorough manner (141) and are especially useful when the research question is not focused.

The five stages of a scoping review have been expanded and detailed by Levac et al. (2010) using the Arksey and O'Malley framework. These include: 1) Identifying the research question, 2) Identifying relevant studies, 3) Study selection, 4) Charting the data, and 5) Collating, summarizing and reporting results (142). An optional stage 6) Consultation exercise to inform and validate findings, is also suggested. The first two stages were particularly relevant to this study: 1) to summarize and disseminate research findings, and 2) to identify research gaps in existing literature. The following will contrast scoping and systematic reviews. Next, the methodology used for identification and extraction of data will be reviewed. Finally, the consideration of standards for comparison, and specifically biomarkers to demonstrate status and efficacy of interventions will be discussed.

# 4.2.1 Scoping Review vs Systematic Reviews

A scoping review follows similar rigorous steps to that of a systematic review, but with a different outcome. Systematic reviews begin with highly focused and well-defined questions, typically only include rigorous study designs, have pre-defined inclusion/exclusion criteria, and focus on the quality of the research findings in order to come to a conclusion; often systematic reviews are used to determine if and how a treatment or intervention should be employed for a specific condition (124,143,144). Scoping reviews are less focused allowing reviewers the ability to address broader topics as compared to systematic reviews (124). Thus, a scoping review is

especially useful when the question is less focused, helping to map out relevant literature in the field of interest (144), including grey literature (124). Due to a lack of prior reviews on this topic, this study did not have a highly specific question, which is one of the key criteria for a systematic review. In addition, this study aimed to explore the diversity of research describing micronutrient status in LTC, regardless of how status was determined (i.e. food intake vs. biochemical markers). Due to the limited work anticipated around interventions outside of oral nutritional supplements (ONS), the scoping review process allowed for the inclusion of various research designs studying micronutrient interventions in LTC. Thus, the flexibility of a scoping review was well-suited to the exploratory nature of this study.

# 4.2.2 Scoping Review Search Strategy Used in these Studies

To enhance the rigor and comprehensiveness of the search, key search terms related to: 1) micronutrient status and 2) interventions to improve micronutrient intake that were specific to the LTC population were identified and reconfirmed with a health research librarian as well as the co-authors. The search included four diverse databases: Ovid MEDLINE, Ovid EMBASE, EBSCO CINAHL, and Web of Science (Table 1). Searches were iterative, and terms were changed, refined and finalized to ensure a comprehensive search. No date restrictions were used to allow for broader inclusion, with December 31<sup>st</sup>, 2012 as the last publication date. Key articles were hand-searched for further citations. This broad search strategy captured both observational and intervention studies, and was later divided as two papers to allow more in-depth descriptions of citations that addressed the two research questions.

#### Inclusion and Exclusion of Citations

There are two key points at which bias can occur in a scoping review; the inclusion of research and the extraction of data (145). To ensure rigor, two assessors were involved in the initial review of citations that were identified in the search. Inclusion and exclusion criteria were applied to all titles and abstracts; where agreement was not reached, a senior author reviewed the citation to determine inclusion. In some cases, a full article review was required to eliminate articles and the extraction process described below also resulted in the removal of some citations as the questions and search criteria were refined. For example, menu analysis studies were initially identified and upon extraction of pertinent data, found to be too dissimilar to food intake and biochemical marker studies to be included in the first scoping review focused on micronutrient status.

To be included, citations of observational studies had at minimum, to report the results of the assessment of one or more micronutrients for a LTC sample, whether based on food intake assessment or biochemical markers representing specific nutrients. Citations of intervention studies had to include, at minimum, results of the effects of supplementation of one or more micronutrients in pill or food-form for a LTC sample. For studies examining multiple participant groups (e.g. community, retirement and LTC participants), only results specific to LTC residents were included and if results were merged across sectors, the citation was excluded. Studies using ONS were also excluded, as these provide macronutrients as well as micronutrients, and effects of micronutrients alone could not be ascertained. Citations were limited to the English language and studies conducted in North America, Europe, Mediterranean (Greece, Italy, Portugal Spain) and Scandinavian countries (Denmark, Finland, Iceland, Norway, Sweden), New Zealand, and Australia. It was anticipated that there would be differences in foods consumed,

LTC nutrition care processes, and micronutrients of interest in other geographic regions. A flowchart of the number of studies examined and included is found in Figure 1.

#### Data Extraction, Categorization, and Synthesis

As extraction is another point at which bias or inaccuracies can occur, it is important to include a second reviewer to check extraction material (146). Pertinent information was extracted to a spreadsheet, and 100% of the articles were divided and reviewed among the authors to validate this extraction. Data extracted included participant characteristics (age (mean  $\pm$  standard deviation), study design (sample size, length of study, intervention type, dosage; for fortification studies), assessment methods (dietary intake assessment method used, biomarkers used), and for the intervention studies, changes identified in outcome variables for both intervention and control groups (for fortification studies). Observational studies focused on status were divided into two categories for summarization, results based on food intake data and those based on biochemical makers. Intervention studies were also divided into two categories, depending on whether the intervention was delivered in pill-form or food form. As anticipated in the methodology described by Arksey & O'Malley, this was a truly iterative process with citations being re-examined for inclusion post extraction and the data extracted being refined several times to enhance presentation of a concise message and overview of the research to date. The senior author also worked iteratively with the candidate to confirm extracted material during the writing of these reviews to ensure accuracy and consistency in reporting.

# 4.2.3 Standards used for Comparisons: Focus on Biomarker Reference Ranges and Cut-offs

To determine adequate intake and status of micronutrients, the Dietary Reference Intakes (DRIs) and biomarkers are commonly used (33,39). This section will focus on the biomarkers, as

DRIs were briefly introduced in Chapter 2, and further discussed in section 4.3 with respect to the menu analysis conducted.

Biomarkers of exposure, that reflect dietary intake, commonly assess blood levels or pools of micronutrients (32). However, this provides only a limited view of 'status,' as it does not allow determination of functional outcomes related to the nutrient's role in the body (e.g. rates of fractures); as such, blood levels can only be considered as intermediate outcomes. Yet, limiting studies for review to only those with functional outcomes would have resulted in few articles that may not have addressed the primary research objectives. Thus, the primary outcomes used in the scoping reviews to address Objectives 1 and 2, used the end point of serum or plasma biochemical markers of nutrients.

The American Medical Association (AMA)'s reference ranges, which are commonly used in both scientific and medical settings, were used for comparison of serum or plasma biochemical results from observational and intervention studies (44). Since AMA provided values for normal ranges, values from the Centers for Disease Control and Prevention (CDC) (45) were also included to provide reference ranges for values that were considered to be below normal (low and deficient values). It is important to note that AMA ranges are often wide and may overlap CDC values. For instance, AMA normal ranges for vitamin D are 35-150 nmol/L, whereas CDC values to determine deficiency are <30 nmol/L, inadequacy is defined at 30-49 nmol/L, and sufficiency at 50-75 nmol/L. Hence, discrepancies may be seen in the categorization of micronutrients when using these two standards. Thus, categorization of low or adequate status by nutrient are based primarily on AMA values for these scoping reviews. Where neither AMA (44) nor CDC (45) reference values are available, as in the case of studies that report results from rare biomarkers, the reference values from the original study were used.

#### 4.3 Menu Analysis

#### 4.3.1 Overview of Menu Selection

In Canada, all meals and snacks are provided for residents in LTC; hence, careful menu planning is needed to ensure residents meet their nutritional needs (25,48,147). Energy, macroand micronutrient analysis of menus is a method to determine whether foods provided in a LTC meet dietary recommendations (48).

In this analysis a convenience sample of menus was obtained for analysis. Registered dietitians and/or nutrition managers part of the acceptability testing (Objective 4) provided the first week (7 days) of their LTC home menu, including recipes and serving sizes, for analysis. Five regular (non-therapeutic), regular texture menus were selected to ensure regional representation, with one specific cultural group included. Homes that provided menus were either stand-alone or part of a small network of homes; none were part of a corporate chain. Ten menus were provided and five were chosen to represent provinces, type (for-profit (FP)/not profit (NFP)) and to promote diversity (i.e. culturally defined population). Further details are not provided to ensure confidentiality of Homes where analysis was completed. One Home menu from British Columbia (NFP), Nova Scotia (NFP), Alberta (NFP) and two from Ontario (1F, 1NFP) were selected; the second home from Ontario included a unique cultural group. This number was chosen to ensure feasibility, and provided greater diversity and a more comprehensive analysis than conducted to date (5,48). As homes may not have the same therapeutic diet menus (e.g. diabetes, low-sodium), and may use different methods or products for modified texture diets, the use of regular (non-therapeutic) was only completed to support comparisons. Key steps in this analysis to improve accuracy of results will be reviewed below.

## 4.3.2 Choice of Nutrient Analysis Programs : ESHA Food Processor & EaTracker

Different criteria for how to choose and perform appropriate nutritional assessments have been established (31,148). Since the menu analysis required use of a nutrient analysis database, it is essential that an appropriate one be selected. Gibson (2005) recommends that the database chosen should represent the average composition on a "year-round, nation-wide basis" (Gibson, 2005, pp. 69). The USDA Nutrient Database for Standard Reference is one of the largest databases of food components, and the majority of foods on Canadian Nutrient File (CNF) is derived from this source, with adjustments where fortification and enrichment practices differ (31). All menus were analyzed using the ESHA Food Processor SQL (version 10.12.0, ESHA Research, Salem, OR, 2012) nutrient analysis program. The analysis examined calories, protein, fibre, and 21 micronutrients. The ESHA program was chosen as it contains a comprehensive database of 55,000+ food items from the most up-to-date USDA database references, manufacturer and restaurant data, and literature references (149). To contrast, the CNF contains only 5000+ foods(150). This program was chosen as it is commonly used in Canadian research involving LTC (48,70,119,151) and in LTC practice, and is based on a comprehensive foods database (U.S. Department of Agriculture (USDA)), including Canadian foods which vary in their production and/or fortification.

Initial food selection from the data base were USDA food choices as these provided the most complete micronutrient data and greater choice of food products. Micronutrient values of American foods were compared with Canadian food product values using the CNF to account for different food supply and fortification practices (152); Canadian foods were chosen where discrepancies existed. Specific foods that required adjustment or replacement to CNF micronutrient values were oatmeal, cream of wheat, corn flakes, and bran flakes; margarine, yogurt, 1% and 2% milk; and eggs. For mixed dishes (e.g. lasagna), recipes, descriptions, or

brand names of purchased products were obtained from the homes to ensure accuracy in analysis. For single food entrées (e.g. chicken nuggets), a similar Food Processor item was selected. Where recipes were not provided, generic recipes used from food distribution companies (e.g. Sodexo or Sysco) or from online recipe databases (e.g., allrecipes.com, canadianliving.com) were used. The Dietitians of Canada's online eaTracker diet tracking tool was used to count CFG servings in menu items and recipes (153). As well, the micronutrient analysis provided by eaTracker, which is based primarily on CNF, was used to confirm the nutrient analysis resulting from the Food Processor program. No adjustments were needed based on this comparison. By searching the CNF for key foods where fortification was different and comparing the complete analysis to eatTracker, these steps improved the confidence in the accuracy of analysis and characterization of the menus.

Confirmation and verification with the home after the recipe was analyzed was done to help ensure the recipe's accuracy. Analyzed menus were provided to the homes for verification and adjustments made as required in portion size or selection of standard items in the food database. All homes were notified to respond via e-mail if changes were required to the recipes used; after two e-mail reminders, it was assumed that no changes were required to the two Homes' menus. Adjustments post analysis were made for three of the five homes based on feedback from site personnel. This member validation and check is important as it enhances the credibility of the study.

# 4.3.4 Interpretation of Micronutrient Analysis of Long-Term Care Menus

The Dietary Reference Intakes (DRIs) were used to interpret and compare and contrast nutrient analysis of home menus to determine adequacy of intake of micronutrients. The micronutrients examined were: Vitamins A, D, E, C, B6, B12, Thiamin, Riboflavin, Niacin,

Pantothenic acid, Folate; and minerals: Calcium, Copper, Iron, Magnesium, Manganese, Phosphorus, Potassium, Selenium, Sodium, and Zinc. Menus' nutrient values were compared to Recommended Dietary Allowances (RDAs)/Adequate Intakes (AIs) for individuals aged 70 and above. Cut-offs of <50% (also known as the Estimated Average Requirement (EAR)) and 50-99% RDA were chosen to demonstrate where Homes' menus fell short of RDA/AIs. Although the EAR is recommended to assess inadequate food intake for groups, it requires data of individuals' usual intake in the group (154). However, only pooled data was available in the studies identified from the scoping review. Thus, the RDA/AI was chosen. Understanding that the RDA, being set at a level to meet 97-98% of the group's requirements (154), may overestimate the proportion of the group at risk, this study established levels of comparisons at 50% of RDA (which is similar to EAR levels) and >99% (above) the RDA, to determine the variations in the groups' intake. Intakes were also compared to AIs, but it is important to note that while mean intake levels at or above the AI can be assumed to indicate low risk of inadequate intake, levels below the AI cannot be assumed to be inadequate (154).

Each home's data was analyzed separately and compared across homes. All home results were also averaged and compared to the DRIs. Food items per day and per week were also entered into EaTracker to determine whether homes met CFG portion recommendations on a daily and, when averaged, weekly basis; only qualitative and quantitative comparisons were made for this interpretation of the diet quality.

# 4.3.5 Development of Super-menus

The purpose of the Super-Menus was to determine if micronutrient recommendations could be met by increasing the nutrient-density of foods alone and providing a smaller volume (regardless of financial cost), given that decreased energy intake with aging is a common phenomenon associated with changes in body composition and decreased activity (59). To date,

no published work on creation of super menus was available as a template. Thus, the criteria set for super-menus for this study were that: 1) foods had to be common foods available to LTC or be comparable to an item served (e.g. beef stew for Irish stew) based on menus provided from Homes from menu analysis, 2) that total volume of a Super-Menu day should be less than or equal to the volume of foods served in the Homes' menu (based on volume or weight to volume conversions of foods served per day), 3) the distribution of food has to reflect that of LTC (e.g. hot cereals at breakfast, soups at lunch, dessert at lunch and dinner, beverages at every meal), and 4) if possible, to include food preferences noted from the focus groups (e.g. cream soups, soft vegetables). Strategies to achieve nutrient-dense recipes included identifying higher micronutrient ingredients (e.g. soup made with milk vs soup made with water) and preparation method (e.g. steamed vs boiled vegetables) options from ESHA, and identification of nutrientdense ingredients, such as herbs and spices, that could be easily incorporated into recipes without increasing the food volume. Planned Super-Menus did not consider cost in their creation.

Super-menus based on commonly served foods across Homes' menus (e.g. hot cereals, quiches, soups) from the above menu analysis, were subsequently created to meet the RDAs for 11 micronutrients (thiamin, riboflavin, niacin, B6, folate, B12, C, D, calcium, magnesium, zinc) that were known to be poorly consumed by older adults in LTC (27,95,116,155–158) and identified to be potentially problematic from the first scoping review. Five daily menus were created to demonstrate the variety that could be achieved in menu planning, including vegetarian options. From the menu analysis, herbs and spices were found to contain high levels of micronutrients and thus those consistent with recipes common to LTC were included. Some food items were also found to have different micronutrient contents depending on the variety [e.g. 1 cup red bell peppers (higher in vitamins A, C, and E) vs. green peppers; 1 cup white beans (higher calcium, potassium, and zinc) vs. black beans], and where appropriate, the most nutrient

dense variety was selected for the Super-menu. Development of these menus was an iterative process to identify feasible micronutrient dense products that did not provide excessive calories and volumes. The five super-menus' micronutrient content was analyzed with Food Processor and EaTracker and averaged for comparison to the five selected homes and the DRI.

#### 4.4 Assessing Acceptability of a Micronutrient Fortification Strategy

Three stakeholder groups were chosen to address research Objective #4, focused on determining the acceptability of a fortification strategy for LTC. These groups were: staff, expert key informants (KI), and LTC residents and families. Methods were chosen based on the stakeholder group involved, to ensure a quality data collection. For staff and residents/families focus groups were the chosen methodology. Focus groups are used as a method to gather individual and interactive opinion and attitudes through a carefully planned framework of questions and discussions (159). The group format allows for interactions and discussions among participants and can contribute to further development of ideas and concepts (159). Key informant interviews were chosen as the method for in-depth discussions with stakeholders who were knowledgeable about key aspects of the proposed strategy. This one-on-one data collection method allowed for flexibility and depth in questioning that was not feasible with the focus groups. This study underwent ethical review and clearance by the Office of Research Ethics at the University of Waterloo (Ethics review #: 18558, Appendix A).

#### 4.4.1 Webinar Focus Groups with LTC staff

Perspectives from diverse participants across Canada were desired for this stakeholder group. As a result, a technology that would support conduct across different geographic regions was required. Webinar focus groups allow for the real-time, immediate response of traditional focus groups, without the physical presence and the need to travel (160). Webinars have been

previously used for training of staff (161) and students (162,163) and were thus considered a viable option for conduct of these focus groups. Online focus groups were conducted with webinar technology (WebEx<sup>™</sup>, Santa Clara, CA)), a program that allows for teleconferencing at the same time as presentation on the internet (164). The webinar format traversed geographical barriers and allowed participants to join regardless of time zone or location. On-line webinar technology offered the opportunity for on-screen presentations, group discussions, and real-time polling questions to engage all participants.

Lower numbers of participants are recommended for online synchronous (real-time sharing) focus groups (165), and telephone focus groups (Krueger, 2014). Thus, several small focus groups (3-7 participants) were scheduled and conducted. Additional techniques for telephone focus groups that transfer to webinar focus groups include shorter duration of sessions (e.g. 1 hour or less), and occasional use of round robin responses to ensure active participation from all members of the focus group (166). Webinar focus groups were conducted with frontline nutrition staff, providing insight into both clinical and production issues with micronutrient fortification. The target participants were dietitians, nutrition managers and chefs working in LTC recruited through the Dietitians of Canada Gerontology Network and the Canadian Society of Nutrition Management (CSNM). Interested participants were sent an invitation e-mail containing: a detailed information letter outlining the purpose of the study and process, instructions to register, and a link to a pre-session online registration survey to collect pertinent demographics. Snowball sampling was also employed; participants of the initial webinars were asked to suggest potential further participants. The recruitment package is found in Appendix B and C. Challenges and benefits of these strategies will be discussed below.

Through consultation with an advisory group consisting of experts from the University of Waterloo and University of Guelph (in applied nutrition, food science, nutritional biochemistry,

and human health and nutritional science), focus group questions were developed (Appendix D). Open-ended questions with additional probes were used as a guideline to solicit information and discussion (167). Questions (with probes removed) were sent prior to the webinar session, as was recommended for non-in-person focus groups (e.g. telephone focus groups) (Krueger, 2014). Polling questions examined nutrients of concern for residents, current strategies used to address micronutrient needs, and participants' ratings on the appropriateness, feasibility and potential effectiveness of a micronutrient fortification strategy. Initial sessions were conducted by the first two authors. Sessions were recorded to allow for transcription of the discussion. During the session, participants were provided with an online Powerpoint presentation on Micronutrient enhancement of food in long-term care homes, created by the candidate and revised by the senior author (see Appendix E; See Appendix F and G for the webinar feedback and thank you letters). The majority of online focus groups have used the chat forum format (160,168) where participants respond to questions via text-based discussions, either as posts or in real-time (169). In these webinars, polling questions were used to elicit initial feedback on key questions and to stimulate discussion. Questions were used throughout the power point presentation.

As no literature was available at the time of the start of this study (September 2012) focused on using webinars as a research method, a feedback survey was used to understand the challenges and benefits of this technology from the perspective of the participants. This feedback was reviewed concurrently with data collection and recommendations were used for adjust subsequent sessions accordingly. The key challenges identified by these participants in the feedback survey (n= 38) are noted below.

General challenges to in-person focus groups include: dominating speakers, "constructing the other," and "tendencies towards normative discourses" (Krueger, 2002; Smithson, 2000; Wright, 2006). Additional limitations proposed for online focus groups include: the requirement

of participants to have access to relevant technology, lack of face-to-face interaction, and difficulties in tracking non-response (i.e. filling out feedback surveys where responses are anonymized and gathered into an online database; more detailed questions were used for sorting categories (e.g. work position)) (160,165). Limitations specific to webinar focus groups are: the need for a mic and quality speakers/ audio system for moderators and participants and preparation for technological set-backs (e.g. back-up recorder).

Dominating speakers often exist in focus groups of any format (170), but are potentially more difficult to manage with lack of face-to-face interactions in a webinar where non-verbal communication is not available (e.g. turning to face another speaker to signify the desire for another participant to speak) (159). Another challenge was "constructing the other," where the nature/characteristics of the moderator (e.g. female dietitian) may lead others in the group to feel as though they are the 'other' (170). Finally, "tendencies towards normative discourse," where participants may desire to comply to a societal norm and avoid discussion of controversial topics (170) continues to be an issue with all formats of focus groups. Details of specific issues and strategies used to overcome these challenges are discussed below.

In the thesis, specific strategies used to minimize having dominant speakers take over discussions in the group, were a) creation of homogeneous groups with enough variation to allow for discussions (e.g. by occupation, by location, etc.), b) keeping the groups few in number (< 5), and c) calling on participants in a round-robin fashion for their opinions and thoughts. An advantage of online focus groups is that face-to-face interaction is eliminated, increasing anonymity, which may allow some participants to feel more at ease and to share (165). Both moderators were female dietitians by profession, which meant that they were more closely related to one group of participants (i.e. registered dietitians), than the others (e.g. cooks, nutrition managers). To avoid being seen as from a select group with expertise, sharing their

perspectives' was minimized and participants' discussion was cultivated through probing and follow-up questions. They also drew on their range of experience in LTC to provide relevant examples and points to solicit further discussion. Moderators took a naïve stance, promoting the participants as experts, which also helped to build rapport and put them at ease. Moreover, moderators also highlighted diverse voices in the group. For instance, when homogeneous groups were not possible due to participants' availability, and only one cook was in a group with dietitians and nutrition managers, the moderator purposefully directed questions to this individual, such as asking, "From your experiences as a cook, what might be some issues with adding fortificants to this food vehicle?" This directed questioning method may be necessary for webinar focus groups, to facilitate more equal contribution from participants. Regarding "tendencies toward normative discourse," the use of probing questions helped to lead participants to think deeper and more critically toward their responses (173). For example, the probing question, "What are foods almost all residents will consume?" helped participants to see a range of possibilities. Finally, participants had the opportunity via email or the feedback survey to provide further comments to the moderators and many took advantage of this opportunity.

Limitations of online focus groups were noted in this research. Recruitment happened through the Dietitians of Canada Gerontology Network and the Canadian Society of Nutrition Management (CSNM) where interested participants contacted the researchers and were sent an email invitation. This automatically limited potential participants to individuals attached to these organizations who had email access. This likely explains part of the under-representation of cooks for these focus groups. Dietitian and nutrition manager participants were encouraged to invite their cooks, but there continued to be low representation. This may also have been due to lack of down time for cooks to participate in the focus groups. Although timing of focus groups

was dictated by participants' hours, the times selected may not have coincided with cook schedules. Alternatively, the low participation of cooks may have been out of lack of interest for the topic, concern about power issues within the focus group, lack of experience with the webinar technology, or lack of access to a computer for participation.

As with all online focus groups, the lack of face-to-face interaction continues to be a limitation (160,168), as participants cannot view others interactions, potentially resulting in limited discussion. Transcripts from these webinars were brief, suggesting that this was a real limitation. Webinars have generally been used for instructing, where trainers broadcast information, and attendees receive information (161). While it is possible to do video-conferencing to see all participants, the researchers decided that sessions of greater than three participants may be too difficult for this format and it was anticipated that staff may not be fully comfortable with this technology. Furthermore, not all participants have web-camera access. It was decided the use of a Powerpoint presentation would help focus attention and engage participants.

While webinar focus groups help with increased interactions between participants by allowing for audio, it presents with its own challenges and limitations. These included issues with audio and technological set-backs (e.g. issues with online recording). The WebEx<sup>TM</sup> program (164) was used in this study. WebEx was chosen for its reliability, as it is known as "the oldest, best-known popular web-conferencing solution" (174) and is commonly used for web-based training and business teleconferencing. As research studies using WebEx were not identified, one main challenge was in managing the technology. Below is the step-by-step strategies taken to meet webinar audio challenges.

Initially, this study proposed an online telecommunication format for talking. However, after several practice sessions, the authors identified that online calling with use of the computer

audio only created feedback noises in sessions with greater than three participants. Thus a phone line format was adopted. This then required the purchase of calling cards for international calls (toll-free calling option did not apply in Canada), as WebEx<sup>™</sup> is a U.S. company. Online calling cards (CiCi) were used. Call-in codes and detailed instructions were e-mailed to participants (e.g. participants from different cities were provided city-specific dial-in numbers). A practice sign-on session was set for one-week prior to the actual session to ensure participants' were acquainted with and prepared for the Webinars (e.g. WebEx player downloaded). Times for focus groups were set with a suggested start-time of 15 minutes prior to session to avoid delays due to sign-on problems. Session 1 and 2 were 15-30 minutes longer than the advertised 1-hour session, as participants had problems with sign-on, and moderators waited until most participants were in the session prior to starting. In subsequent sessions, the moderator would send one reminder email 5 minutes after the session began for participants who did not sign on, and begin the session to remain within the 1-hour session time.

In the first few sessions, participants were offered the option to use online calling or phone-line/calling cards. However, issues with hearing lead to the recommendation that all participants use a phone line for dial-in. Several participants had issues with volume (e.g. no mic for phone) during the session, and responded via chat. The chat option was also used if participants had additional comments on previous question topics, and allowed for documentation of additional comments without stopping the group to return to the previous topic. Participants had the option to share chat comments with the moderator-only, or everyone in the session.

The WebEx<sup>™</sup> program provided an immediate recording option. However, due to a glitch in the program, the audio was lost for the second session. While WebEx<sup>™</sup> agreed it was an issue on their end, and technicians were contacted, they were unable to retrieve the audio.

Since the majority of the changes were made in the first two webinar sessions to facilitate the flow of the sessions, it was decided that the first two sessions would be used as trial sessions and not transcribed. However, the polling and feedback responses from these two sessions were included in results as the question content was similar. To avoid this problem in future, the researchers added a back-up external recording device to each session, so two audio recordings were made to avoid the risk of lost sessions.

After the webinar, participants were emailed a link to a feedback form, which allowed them to provide further comments on the topic as well as to rate their experience with the webinar format and technology. Results from participants' feedback provided insight into how to run smoother sessions. For instance, noting that participants commented 'sessions were a bit rushed,' and 'using the chat option helped,' allowed the researchers to modify flow and encourage use of the chat option in subsequent sessions. Confirmation from the subsequent feedback questionnaires also ensured that the process was working; for example participants agreed that the 1-hour session was an appropriate length.

Due to the small numbers of participants for each focus group, several focus groups were conducted (n=11) over a 2-month time frame. This allowed for the conduct and analysis of findings to be an iterative process (159), which is not available with chat forum focus groups (160). Thus, despite set-backs with the initial webinar focus groups conducted in this study, with proper preparation they may be closer to in-person focus groups while allowing the ease of the online-format as compared to chat forums.

#### 4.4.2 Key Informant Interviews with Relevant Experts

It was anticipated at the outset of this research that diverse perspectives would be required to address the issue of acceptability of fortification in LTC to meet micronutrient needs.

It was also anticipated that some individuals may have unique and deeper experience than staff focus group participants and an opportunity was needed to capture these perspectives. Key informant (KI) interviews have been described as a method to gather in-depth information from an expert source of information in a less structured interview format (175,176). Tremblay (1957) has identified five criteria for the "ideal" key informant: 1) Role in the community (continuous exposure), 2) Knowledge (direct access to information sought), 3) Willingness (to communicate knowledge), 4) Communicability (able to communicate in an intelligible manner to the interviewer), and 5) Impartiality (have minimum personal bias, and to communicate any existing biases to the interviewer to allow proper appraisal of information obtained). How these objectives were achieved is detailed briefly below, and in detail in Chapter 8 on acceptability testing.

From the webinars, a number of participants who were knowledgeable on the topic of interest (i.e. had conducted fortification) were identified and invited for individual in-depth Key Informant (KI) interviews. As well, the advisory committee provided recommendations on various stakeholder groups whose insight and opinion on the potential strategy was desirable and should be solicited. (e.g. government, food industry). KIs were identified and recruited by the candidate via email and those interested in participating were sent an information letter outlining the expectations for an interview and the study process. Due to the likely small sample of possible KIs, recruitment is usually by a convenience sample (177) (See Appendix H and I for Key Informant Interview information letter and question outline).

KI interviews provided an opportunity to attain more in-depth information addressing questions with respect to the feasibility of the developing strategy that arose from the webinar focus groups. They were all conducted after the majority of staff focus groups were completed; the senior author conducted most of the interviews, while the primary author took notes, as it was

anticipated that each line of questioning used with participants could be unique and an interviewer with greater experience in research content was desired (178). The KI interviews were done in an iterative process, where discussions with one expert (e.g. dietitian in a distribution chain) led to another that could provide responses that the previous expert could not answer (e.g. nutrition manager of the distribution chain). Thus, due to the diverse expertise of KIs (e.g. Ministry of Health staff, distribution chain staff, director of sales in nutrition management products), while the KI question guideline was used, question order changed due to flow of the discussion, and additional questions were added depending on the expertise of the KI. These on-the-spot added questions were in lieu of probing questions used in webinar focus groups and provide strength to the methodology (179,180). This flexibility is essential when interviewing various KIs of diverse expertise, and worked well in this study. As with webinars, digital recordings were taken of these interviews and transcribed verbatim for analysis. Interviews were typically one-hour in length.

# 4.4.3 In-person (Traditional) Focus Groups with Residents and Family Members

Although webinar and KI informants were generally in favour of a fortification strategy in that they saw this as a viable strategy if certain issues were addressed (e.g. adequate staff training, feasible cost of fortified food), the majority of feedback centered on the production and Homes' perspectives, yet acceptability from the end users (i.e. residents) had yet to be established. Thus, resident and families' views were ascertained via in-person focus groups (See Appendix J-L for resident/family focus group information package, consent form, and feedback forms).

Due to the limitations in gathering residents for focus groups (i.e. difficulties in traveling, lack of internet and other technology required for in-person focus groups, difficulty hearing on

the phone), the traditional, in-person focus group format was adopted for the resident/family focus groups. Benefits of in-person focus groups include allowing moderators to assess the degree of attention that participants are giving to the discussion (166). This is especially important for conducting focus groups with vulnerable populations (e.g. children, elderly), as being in the same room and seeing participants face-to-face allow moderators to pay better attention to the participants to address any issues that arise during the session (181). For instance, the moderators in the in-person focus groups conducted in this thesis found that certain participants had difficulties reading the ethics form, and moderators or staff had to read this out to them. Moreover, the moderators learned that silence in the group may indicate that the residents could not hear the question or did not understand the use of certain terms or the concept in the question, and not that they did not have comments on the question. Taking pauses and probing to see if participants needed definitions of certain terms or elaborations on concepts helped to address these issues in our resident/family focus groups. Further, focus groups were preferred by vulnerable groups over one-on-one interviews, as the group format is perceived as less threatening (181). Thus, in-person focus groups was the ideal choice for gathering resident and family's perspective of a potential food fortification strategy in LTC.

In-person focus groups were conducted at five LTC homes to obtain the opinions of family members and residents; these were done in the late summer and fall of 2013, post completion of all webinars and most KIs. Due to geographic constraints, only sites within an hour of the University of Waterloo were recruited. Initial contact was made by phone or email to nutrition management/dietitians to determine interest. Recruitment posters/letters were provided to notify potential participants of upcoming sessions. Group discussions were scheduled at the routine resident/family council/food committee meetings and a 20-30 minute time slot was allotted to the discussion. As a result, staff members were also present, although their opinions

were not elicited; they acted as supports to the researchers for completing consent forms and helping with hearing impaired individuals.

Participants signed consent forms prior to the session and completed an anonymous feedback questionnaire on benefits and concerns about the strategy at the end of the session. The feedback questionnaires was part of the methodology, as it was anticipated that the short 20-30 minute session time slots given by the Homes may not be adequate to capture the resident/families' comments, or residents may not be able to express themselves adequately or quickly enough during the session. Thus, the questionnaires provided an additional forum and opportunity to capture afterthoughts of the fortification strategy, as not all participants spoke during the discussion. These sessions were not audio recorded to keep the discussion informal and allay any concerns about confidentiality of the information, as well as challenges with soft-spoken participants on the digital recording. Extensive notes were taken by one of the two researchers present to enhance credibility.

# 4.4.4 Enhancing Rigor of Qualitative Methods for Acceptability Testing

This study used a combination of quantitative and qualitative methods. It is important to establish validity of the study, to ensure that findings are supported by evidence (182). Rigor in qualitative research has been called an assessment of its 'trustworthiness' (183). Four criteria for establishing trustworthiness of qualitative research have been established by Lincoln and Guba (1985). These terms have been compared to quantitive terms (in brackets): 1) credibility (internal validity), 2) transferability (external validity), 3) dependability (reliability), and 4) confirmability (objectivity) (184).

Credibility assesses the results such that they are credible/believable to participants and those external to the research (184). Several activities were undertaken to enhance credibility.

Qualitative data from webinars and KIs were transcribed. Inductive content analysis was used to identify common points or concepts, patterns, and variations (185). The candidate and a student researcher each reviewed and coded half of the transcripts to complete an initial overview of the data using open coding (186). A code book was subsequently developed by the candidate, senior author and the student researcher to assist with organization and categorization of the data (187,188). A consistency check was done when independent coders coded raw data to create codes and categories, then compared results to reduce the data (189). Including more than one person and having inter-coder agreement in the coding process helped to enhance credibility of the coded data (190). All transcripts were recoded after the development of the code book using selective coding.

Additionally, external members not immediately involved in the study (134) in the form of a thesis committee reviewed findings and commented on processes to help direct and check the quality and relevance of each step of the research. Use of member or stakeholder checks, where informants are asked whether results represented their experience or whether relevant information was captured from the session helped to keep the findings true to the lived experiences of the participants (189).

The use of an audit trail also helped to enhance to credibility of this study. By providing an audit trail of carefully kept logs, field notes and memos of activities throughout the research process, noting chronological steps, data analysis procedures, and strategies, the researchers enhanced the internal validity of the study (134) as well as its confirmability. Exceptions were also noted to account for possible differences in findings, such as membership in focus groups.

Transferability is the extent to which qualitative research results can be transferred to another context/setting. A strategy to enhance transferability is *thick, rich description*, which describes the context in which the behaviour occurs, so that those reading the description would

feel as though they were in the situation/setting (134). To enhance transferability, multiple respondents were involved and transcription of webinars and key informant interviews provided opportunity for in-depth analysis of findings, and thus this rich description. Quotes were identified to exemplify these rich descriptions in the manuscript based on this work. With these descriptions, the reader can then decide whether or not the findings can be applicable to another similar setting, or the greater population (e.g. other LTC Homes in Canada or internationally). Data saturation can also demonstrate transferability. Saturation was achieved between webinar focus groups and KI interviews, as one-on-one interviews identified the same challenges mentioned in webinar focus groups. While this was not the initial purpose of including multiple perspectives to answer our research objectives, the identification of data saturation helped to verify the transferability of our findings.

Data from the three groups of diverse stakeholders was integrated in this acceptability study (187,188). *Triangulation*, to be discussed further below with respect to the acceptability study as well as across all studies conducted in this thesis, also promotes transferability. Triangulation is the analysis of data from various sources of separate and dissimilar information (e.g. focus group interviews, feedback surveys) in order to categorize the data and generate common themes and understanding (134,182,191). Analyses of these multiple sources of evidence using triangulation, and the congruent findings (i.e. issues with micronutrients in LTC), provided evidence for the need to address micronutrients in LTC, and help strengthen external validity or transferability of the overall study (182).

Dependability of the data signifies the replicability or repeatability of the study (134,184). As discussed above, the audit trail provides a basis for replicability, as well as a transparent process written up in the manuscript for data collection, analysis and interpretation. Use of post-interview notes also enhanced dependability. External auditors could use these

documents, transcripts and the manuscript to determine if the process was logical, determine potential for biases, and whether or not the data is credible.

Verbatim transcription allows for interpretation of qualitative data and prepares the data for analysis (192) and ensures dependability of the data. However, errors could be introduced during the written transcription stage; Poland (1995) identified more than half of professionallytranscribed passages contained significant transcriber errors. By having the research candidate (IL), who was also the moderator, transcribe the recordings, the amount of errors are likely reduced, further promoting dependability.

Lastly, confirmability describes the objectivity (neutrality) (189), and the degree to which the results can be confirmed or corroborated by others without researcher bias or distortion (184,193). The use of 'Researcher Reflexivity,' where researcher bias is minimized by first having researchers understand their own position through identifying and reporting their personal values, assumptions, and biases at the start of the research and to determine how this may affect the conduct of the study is another activity that supports confirmability of the research (Creswell & Miller, 2000). This critical paradigm also takes into consideration the impact of social, cultural and historical contexts. Since the topic of micronutrients in LTC was new to the research candidate, this may have minimized research bias, yet as a dietitian with some experience in long term care, she had a potential bias towards the understanding of malnutrition which could have influenced interpretation of findings. To account for this bias and that of other investigators, inclusion of a multi-disciplinary thesis committee to review and comment on findings helped to challenge these biases. The scoping review at the start of the study also provided the research candidate with broader view of the issues with micronutrient food fortification in LTC; by understanding the historical context, and the benefits and challenges other researchers have faced, this reduced individual researcher bias due to her clinical experience.

The rigorous methods of data collection documentation and audit trail, transcription and analysis throughout the study also served to enhance confirmability of the study. Lincoln & Guba (1985) have cited six categories of reporting information for developing the audit trail (194). These were: 1) Raw data, 2) Data reduction and analysis products, 3) Data reconstruction and synthesis products, 4) Process notes, 5) Materials relating to intentions and dispositions, and 6) Materials relating to intentions and dispositions. These steps were carried out for the acceptability testing study. For example: Raw data (notes and memos written, feedback survey results) were first collected. Next, data reduction and analysis happened when field notes were combined and written-up (e.g. when webinar field notes between the two moderators were compared during peer debriefing, transcription and initial). Next, data reconstruction and synthesis occurred during the coding stage when coders identified, confirmed, corrected, and reduced findings to emerging themes and categories. Two coders were involved to lend credibility to this step. Process notes (methodological notes, audit trail notes) were kept throughout this process. Materials relating to intentions and dispositions were kept, including personal notes for decisions made and expectations of the study (e.g. prediction of results). Lastly, instrument development information was also kept, including earlier formats of the PowerPoint presentation and discussion questions and later versions after changes were made (e.g. putting 3 polling questions on one slide in the final PowerPoint presentation). These detailed steps ensure that decisions made were transparent, and potential biases were minimized.

Confirmability is also enhanced by comparing findings of qualitative and quantitative studies where similar conclusions are reached (189). Thus, a final step in confirmability is the triangulation of findings across stakeholders and forms of data collection (e.g. polling questions, rating questions and quotes) which will be discussed further below.

# 4.4.5 Overview of Data Analysis, Interpretation and Triangulation of Acceptability Data

This next section will provide an overview of the data analysis process and its interpretation, as well as describe how stakeholder data was triangulated for the acceptability of food fortification in LTC study. Several steps were taken to triangulate data from these diverse perspectives and forms of data collection. To begin, polling data from staff webinars were integrated into the subsequent discussion that occurred during the session. Data from pre-session registration surveys, online polling questions, and post-session questionnaires were summarized and interpreted with descriptive quantitative analysis (e.g. percentages of participants working as dietitians), and where appropriate, triangulated with qualitative data. For family/staff focus groups, the feedback form confirmed the qualitative data captured during discussions and the rating was quantified.

The order in which data was collected from stakeholders supported triangulation of findings. Webinars with staff were purposefully chosen as the first form of data collection as the strategy of food fortification was not fully flushed out. Webinars were used as a testing ground for the concept and considerations that would be required. KI interviews occurred next and delved into these issues in more detail. Family and resident focus groups occurred last. By this time the fortification strategy had been more clearly defined in terms of how it could occur and what some of the parameters may be, supporting a more focused discussion with these participants to determine their acceptability of the strategy.

Debriefing occurred after each focus group and KI interview between the candidate and senior author to discuss overall impressions, key points, main areas of agreement or disagreement, and new data that resulted from each session (187). This peer debriefing provided support, identified the researchers' biases, challenged their assumptions, and encouraged critical

thinking of research methods, findings and interpretations (193). Thus, subsequent focus groups and key informant interviews were conducted with the knowledge of results from prior data collection points and were used to not only corroborate but also extend findings.

All webinar focus groups and KI interviews were transcribed verbatim prior to analysis, with identifiable information removed. Transcription was completed by the candidate who was involved in these data collections. This transcription process allowed the research candidate to become re-acquainted with the data and acted as another level of analysis, influencing further data collection and interpretation in an iterative process.

Finally, to summarize the qualitative data across stakeholders, the same form of analysis was completed and data were collapsed across stakeholder groups. These data were descriptively summarized with minimal interpretation (159,187) and are presented as key concepts that address the purpose of the study; specifically i) concerns with micronutrient intake, ii) reflections on current strategies, iii) appropriateness of fortification, iv) promoting feasibility, v) determining effectiveness, and vi) overall acceptability of the strategy. Thus the write-up of this study demonstrates the triangulation of diverse perspectives used to determine the acceptability of micronutrient fortification of food for LTC.

# 4.5 Overall Triangulation of Methods

As various numerous sources of information were collected to address the research question, the data and findings must be systematically analyzed and summarized. Triangulation is a research technique that combines different but complementary sources of data to answer a particular research question (195). Triangulation analyzes various sources of separate and dissimilar information, such as data sources, theoretical comparisons and various methods (e.g. surveys, interviews, collected documents) in order to categorize the data and generate themes (134,191). By comparing results from different methods and data sources, intrinsic weaknesses

or biases of an individual method can validate and/or expand on the other, improving not only the understanding of the research aim, but also the overall credibility of the study (195). Five types of triangulation were identified by Guion et al. (2011): 1) data triangulation, 2) investigator triangulation, 3) theory triangulation, 4) methodological triangulation, and 5) environmental triangulation. Within the triangulation design, there is the choice of convergence model, the data transformation model, the validating quantitative data model, and the multilevel model (195). This study used convergent triangulation, where quantitative and qualitative findings were examined with equal weight and importance (134). A convergence model is used to compare, "validate, confirm, or corroborate quantitative results with qualitative findings" (Creswell & Clark, 2007, pp.65). When the study is well-planned so that both the quantitative and qualitative methods complement each other so that the data converge or triangulate, they enhance completeness and overall quality of the study more than a single method alone (135).

Challenges in using the convergence model of triangulation include the differences in type of data (e.g. scoping review vs. menu analysis), type of samples and sample sizes (195). In this thesis, the candidate has attempted to address an overarching research question with four sub-studies that have different purposes, methods and findings. However, by designing the studies that address an overarching research question such as this, but focused on similar concepts, a merging of data interpretation is possible (182,195). Triangulation across these research objectives will be used to address the overall research objective of investigating micronutrient malnutrition in LTC and strategies to improve micronutrient intake and will be undertaken in the Discussion of this thesis.

Triangulation at the level of interpretation of findings and answering of the broad research question is not the only way in which triangulation occurred in this thesis. Additionally, triangulation occurred at the level of the conduct of the various studies where findings from one

objective impacted the methods and form of data collected in a subsequent study. For instance, the scoping review of micronutrient intake in LTC helped to identify that menus may not be providing adequate micronutrients to meet residents' DRI needs, and resulted in the third objective being added to this thesis. The design of super-menus was focused on those nutrients found to be consumed less than the RDA based on the scoping review.

The scoping review results were also used in the acceptability study. An optional consultation process in scoping reviews is advised (124) and preliminary findings of the scoping reviews were part of the discussion in stakeholder groups and subsequently part of the emerging themes in this acceptability study. Specifically, results from the second scoping review lead to questions on food vehicles to discuss in focus groups and participants then provided input into appropriate foods to include in the strategy.

From the focus groups, it was identified that not all homes have the capacity to analyze micronutrient content of menus, thus menus were collected from webinar participants (LTC staff) and selected menus were analyzed for micronutrient content to address objective 3. Qualitative findings from the acceptability strategy testing, also challenged the researchers to consider more fully food-first approaches before fortification. When it was identified in the five home micronutrient analysis that some homes were closer to achieving the DRI without excessive calories, the process of completing a super menu with the same detail to micronutrient analysis was undertaken.

Of interest are the agreement and disagreements between findings of each of the four components of the thesis. For instance, while certain micronutrients of concern (e.g. vitamin D) were identified across data sets, a wide variety of micronutrients were addressed, such as potassium and zinc with participants from acceptability testing, yet the scoping reviews identified selenium as a micronutrient of concern, which was not mentioned by participants in

the acceptability testing. This leads the research candidate to question whether there is a disconnect between research findings and actual practice, and whether both should be considered with equal weight. Yet, inconsistencies or dissimilarities in findings is not always an indication of error. At this point, it is important to dispel the misconception that triangulation must arrive with consistent results across all data sources. Patton (2002) suggests that these inconsistencies are likely due to the different inherent purposes and strengths of research approaches. Thus, he advises that these inconsistencies should not be used to weaken the evidence, but rather be examined as opportunities to identify deeper meaning in the data (196). For this thesis, inconsistent findings could be used as evidence for the need to determine whether there is a disconnect between research findings and actual practice, and identify whether knowledge translation efforts could be placed to bridge these gaps. Nonetheless, overall findings indicate that numerous micronutrients are of concern, beginning with inadequacies in menu planning, intake, to biomarker status.

#### 4.6 Summary

In summary, four sub-studies each addressing a single objective were designed to address the overall research question on whether or not micronutrient malnutrition is prevalent and how it should be addressed in LTC. Although not a formal mixed methods study, the combination of four separate studies with diverse methods allowed for triangulation of methods and findings enabling a more fulsome answer to the research question. Key points in methods to ensure rigor and quality data collection have been outlined in this overview. The methods specifically undertaken for the acceptability testing have been reviewed to demonstrate that careful planning, implementation, and analyses of these methods enhanced the credibility, transferability, dependability, and confirmability of these qualitative findings.

# Chapter 5

# Micronutrient Intake and Status in Long-Term Care: A scoping review. Abstract

Micronutrient deficiency is a potentially prevalent form of malnutrition among long-term care (LTC) residents, influencing health, function and quality of life. Eating difficulties, taste changes, and decreased appetite often hinder food intake. This review maps the literature on micronutrient consumption and biochemical status in LTC residents. Arksey and O'Malley's scoping review framework was used to conduct, a comprehensive search of four electronic databases. A total of 3342 citations were identified and post screening, data from 50 studies was extracted. Vitamin D, folate, calcium, vitamin E and B6 were identified to be consistently <50% Recommended Dietary Allowance for LTC residents using food intake data. Several other nutrients were consumed at 50-99% of the RDA. More than one study found biomarkers to be low for vitamin D, C, folate, and iron. These findings suggest that micronutrient intake and biochemical status are suboptimal for key nutrients in LTC.

#### KEYWORDS micronutrients, long-term care, intake, status

(Prepared for submission to the Journal of Nutrition in Gerontology and Geriatrics)

# 5.1 Introduction and Background

Older adults living in facilities face particular health challenges with various acute and chronic illnesses (5,21,56). Malnutrition has been well-documented as a factor contributing to ill health in older adults, particularly in long-term care (LTC) (5,23,197). Adequate intake of a varied diet is needed to meet nutrient requirements, but physiological factors including challenges with self-feeding, early satiation, taste changes, dysphagia, and decreased appetite often hinder older adults' food intake, rendering them nutritionally vulnerable (13,14,198). Thus, micronutrient deficiency is purported to be relatively prevalent among older adults living in LTC (5,21,199). As a preventable form of malnutrition, identification of those nutrients most likely to be at risk is a necessary first step. Poor micronutrient (vitamin/mineral) status is known to affect immunity, cognition, functional abilities, and quality of life (17,22,200). Nutrition interventions have commonly focused on protein-energy malnutrition (PEM) (26,201–203), but relatively few treatment options have been explored to address micronutrient malnutrition in LTC. In practice, screening for PEM is more common in LTC than for micronutrient problems, due in part to the nature of developed screening tools, and may further contribute to the difficulty in detecting micronutrient malnutrition in LTC (13,107,198). At present, there is no consensus on the best way to treat poor micronutrient intake in LTC residents (13), and if such treatment will be beneficial.

Logically, the risk of micronutrient deficiencies increases as food intake decreases (5,21,24). Poor food intake is common in LTC (5,21,23), and recent research demonstrates that menus may not provide adequate micronutrients to meet dietary recommendations, even when meals are completely consumed (5,19,24,25). Clearly, a shift towards prevention of micronutrient malnutrition is needed for this vulnerable population. Past research has examined single micronutrients (155,204,205) or combinations of micronutrients targeting specific diseases

(114,206) but less work has been done to assess micronutrient intake and/or status for long-term care residents as a whole. However, there has been increasing focus on population-wide dietary intake and nutritional assessment to further research and develop nutritional policies for vulnerable groups (207). Potential interventions to address micronutrient malnutrition in the elderly population, such as food fortification, has also been researched (29). To move forward, a greater understanding of the micronutrients of concern (i.e. micronutrients that residents are at highest risk of deficiencies for), based on poor intake or biochemical status is needed for the LTC sector. The aim of this study is to identify micronutrients that are poorly consumed or low based on a variety of standard biomarkers (high risk micronutrients) to provide a foundation for potential targets for future micronutrient interventions in LTC.

#### 5.2 Method of Review

A thorough literature review is needed to provide a better understanding of high risk micronutrients for LTC residents. A scoping review was the chosen method, as it provides an opportunity to quickly explore a body of literature, and allows for summary and dissemination of research findings, and identification of research gaps in existing literature (124). Scoping reviews have been recommended for areas of research that have yet to be reviewed in a thorough manner (141). The five stages of a scoping review have been expanded and detailed by Levac et al (142), using the Arksey and O'Malley framework (28). As compared to a systematic review, scoping reviews allow researchers the ability to address broader topics (124), especially when the question is less focused, helping to map out relevant literature in the field of interest (144), including grey literature (124). The flexibility of a scoping review is well-suited to the exploratory nature of this study. In order to enhance the rigor and comprehensiveness of the search, key search terms were identified and reconfirmed with a health research librarian as well as an advisory group. The search included four diverse databases: Ovid MEDLINE, Ovid EMBASE, EBSCO CINAHL, and Web of Science. Searches were iterative, and terms were changed, refined and finalized to ensure a comprehensive search. No date restrictions were used to allow for broader inclusion, with December 31<sup>st</sup>, 2012 as the last publication date. Key articles were hand-searched for further citations. This broad search strategy captured both observational and intervention studies, and was later divided as two papers to allow more in-depth descriptions of each area of study. This paper will only discuss results of the observational studies.

Inclusion and exclusion criteria were applied to all titles and abstracts. Citations had to include at minimum results of the assessment of one or more micronutrients for a LTC sample. For studies examining multiple participant groups (e.g. community, retirement and LTC participants), only results specific to LTC residents were included and if results were merged across sectors, the citation was excluded. Citations with food intake data and/or biomarkers assessing status were included, and were limited to the English language. Studies conducted in North America, Europe, Mediterranean (Greece, Italy, Portugal Spain) and Scandinavian countries (Denmark, Finland, Iceland, Norway, Sweden), New Zealand, and Australia were included; differences in foods consumed, LTC nutrition care processes, and micronutrients of interest in other geographic regions were anticipated and thus studies from other regions excluded. The initial screening process of titles, abstracts and where required full text, was conducted by the first author (IL) with agreement with the senior author (HK). A subsequent title and abstract review process was completed by a second trained reviewer using the same inclusion/exclusion criteria in efforts to avoid missing key articles from the search results. Any articles in question to be included in the review were examined by the senior author and both

authors came to a decision on inclusion or exclusion. Pertinent information was extracted to a spreadsheet, and 100% of the articles were divided and reviewed among the authors to validate this extraction.

# Food Intake

The Institute of Medicine's Recommended Dietary Allowance (RDA) provides a reference that meets nutrient requirements for nearly all (97-98%) of nutrient requirements for a particular gender and age group (e.g. those >70 years old) (28). Intake data was compared to the RDAs (28) for individuals greater than 70 years of age to allow for standardization of resulting data, as other nations may follow their own version of dietary references. Cut-offs of <50% (also known as the Estimated Average Requirement), 50-99%, and >99% of RDA were chosen to denote higher to lower risk of inadequate micronutrient intake. Adequate Intake (AI) values were used where there was no Estimated Average Requirement (EAR) to establish the RDA, and cut-offs for this analysis were set at < AI. RDA cut-offs for males were used if a study provided a combined-gender intake. If the study separated male and female intake values, these were recorded separately. For single-gender studies, the specific gender's reference values were used (i.e. female RDA for vitamin C if it was a female-only study population).

Common intake data collection methods included weighed food records (WFR), estimated food records (EFR), and other methods (e.g. Food Frequency Questionnaires (FFQ), dietary surveys, 24-hour recalls, diet histories). WFR were considered to be better quality than EFR, which was also considered better quality data than the other methods. Studies were categorized based on the dietary intake assessment method used; where a study used multiple dietary intake assessment methods, the study was listed under the highest quality assessment method.

#### **Biomarkers**

Some identified studies provided biochemical data to assess LTC residents' micronutrient status. As citations used a variety of biomarkers with varying reference ranges, to promote comparison across studies, the American Medical Association (AMA)'s reference ranges, which are commonly used in both scientific and medical settings, were used (44). Since AMA provided values for normal ranges, values from the Centers for Disease Control and Prevention (CDC) (45) were also included to provide reference ranges for values that were below normal (low and deficient values). Studies were compared to AMA (44), CDC (45), and the reference values from the original study from the abstraction. To note, AMA ranges are often wide and may overlap CDC values. For instance, AMA ranges for vitamin D are 35-150 nmol/L, whereas CDC values to determine deficiency are <30 nmol/L, inadequacy at 30-49 nmol/L and sufficiency at 50-75 nmol/L, hence discrepancies may be seen when in the categorization of micronutrients by each reference range. Categorization of low or adequate status by nutrient are based on AMA values, or on the original study's values if AMA values were not available.

#### 5.3 Results of Scoping Review

#### Overall

The search strategy resulted in 3342 articles in total (Figure 1). Full articles were excluded if they: focused on disease/treatment (n=11), were not part of the geographic region for inclusion (n=4), the full citation was not accessible (n=12), did not include a LTC population (n=13), did not present micronutrient data (intake or biochemical) (n=26), focused on the use of oral nutritional supplements (n=10), were reviews and not original studies (n=32), or did not address our research question (e.g., menu planning, letters to the editor) (n=25). Baseline micronutrient data for intervention studies were also included. The screening criteria resulted in 50 observational studies, with 34 including dietary intake and 22 including micronutrient biomarkers. Results from these observational studies will be presented as food intake first, then biomarker data.

# Food Intake

The 34 intake studies were quite heterogeneous in their length of data collection, range of micronutrients examined, and size of sample (Table 2). WFRs were used in 16 studies, with a large range in length of food intake collection from 1 (US, The Netherlands) (208,209) to 21 days (Canada) (5). Size of sample ranged from 9 (Canada) (63) to 252 residents (Spain)(210). EFRs were used in 12 studies, ranging from 1 (Australia) (27) to 7 days (US) (50), with the majority (n=8) as 3-day EFRs. Other diet intake assessment methods included FFQs (n=3), 24-hour dietary recall (n=2), and diet histories (n=2). Age of the participants was relatively consistent across these citations with participants ranging between 65 and 102 years; the mean age of participants was approximately 80 years of age. Studies originated from Canada (26%, n=9 of 34), Spain (20%, n=7) and the US (17%, n=6), followed by the Netherlands, Australia, and Sweden, with Austria, Denmark, Finland, and Ireland (n=1 for each). Publication years spanned from 1979 to 2012, with the majority of studies conducted in the 2000s (46%, n=16 of 34), followed by 1990s (n=9) and 2010s (n=6).

#### OVERVIEW OF MICRONUTRIENTS OF CONCERN BY RDA/AI

Less than 50% RDA (or < EAR): Of the 34 relevant studies, the most frequently cited micronutrients <50% of RDA were: vitamin D (n=18 citations; 6 WFR, 11 EFR, 1 Other), folate (n=7 citations; 6 WFR, 1 Other), calcium (n=6 citations; 3 WFR, 2 EFR, 1 Other), and vitamin E (n=6 citations; 2 WFR, 3 EFR, 1 Other) (Figure 2A). Other micronutrients identified in at least

one citation at <50% RDA were: vitamin B6, magnesium, vitamin C, vitamin B12, selenium, vitamin A, iodine, and thiamin.

**50-99% RDA:** For micronutrients between 50-99% of RDA, the most frequently cited were: calcium (n=17 citations; 8 WFR, 6 EFR, 3 Other), thiamin (n=13 citations; 10 WFR, 2 EFR, 1 Other), zinc (n=13 citations; 8 WFR, 5 EFR), and vitamin B6 (n=10 citations; 5 WFR, 4 EFR, 1 Other) (Figure 2B). Others micronutrients with intake between 50-99% from at least one citation were: vitamin C, folate, magnesium, vitamin A, riboflavin, iron, vitamin E, iodine, and vitamin B12.

**Greater than 99% RDA**: The most frequently cited micronutrients >99% RDA were: vitamin C (n=12 citations; 7 WFR, 4 EFR, 1 Other), vitamin A (n=8 citations; 5 WFR, 3 EFR), vitamin B12 (n=7 citations; 5 EFR, 2 Other), thiamin (n=6 citations; 2 WFR, 4 EFR), and riboflavin (n=6 citations; 5 EFR, 1 Other) (Figure 2C). Others with at least one citation indicating adequacy of intake included: iron, niacin, calcium, magnesium, selenium, and zinc.

**Compared with AI:** Micronutrients identified to be below the AI with at least one citation were: potassium and pantothenic acid. Copper was the only micronutrient with an AI cited with intake above the AI (21). Given that this paper is interested in the low micronutrient intake for older adults, elaboration will be provided for the top 4 micronutrients (vitamin D, calcium, foate, vitamin E) where several citations indicated intake that was <50% RDA; citations that did not identify these low levels of intake in these nutrients will also be included in this discussion for comparison purposes.

#### VITAMIN D

All citations, regardless of diet assessment methodology identified vitamin D intake to be consumed on average below 50% of the RDA.

<u>WFR:</u> The 7 WFRs examining Vitamin D originated from Canada, Ireland, Spain, and Sweden, and ranged from 2-7 days in length (3 and 5-day WFRs were most common). Sample size ranged from 9 to 86 residents. Only one study exclusively examined vitamin D and calcium intake (43); all other studies examined vitamin D intake in combination with multiple nutrients. The majority of measurements were taken at one time, although the study by Lammes et al. (211) (Sweden) repeated measures three times over 1.5 years. The lowest WFR intake levels reported were by Moreiras-Varela et al. (212) (Spain), at  $0.7\pm0.2 \mu g$  (male) and  $0.6\pm0.3 \mu g$  (female), and by Vir et al. (56) (Ireland), at  $1.25\pm0.68 \mu g$  (male)  $1.07\pm0.39 \mu g$  (female). However, there was less variability in the remaining 5 studies, with intakes ranging from 3.9 to 5.7  $\mu g$  vitamin D (19,43,63,211,213).

EFR: The 11 EFRs citing vitamin D as a micronutrient of concern were from Australia, Canada, Denmark, and the US. Length of EFR ranged from 1 to 7 days with sample sizes of 30 to 169 residents. Seven of these studies were specific to vitamin D and/or calcium intake only (14,15,27,97,214–217), and the remainder examined vitamin D in combination with other micronutrients. The lowest level of intake was recorded by Nowson et al. (Australia) examining 139 residents with and without eating impairment from 9 different LTC sites; those with impaired eating ability on a pureed diet had lower vitamin D intake (0.7  $\mu$ g) as compared to those without an eating impairment (1.1  $\mu$ g) (27). Further intake analysis of residents on full, soft, or pureed diets found that vitamin D status worsened as the diet became downgraded. Interestingly, this level was lower than the vitamin D intake level identified by Gloth et al. (US) of sunlight-deprived residents who had been confined indoors for 6 months or longer (216). Johnson et al. (US) also found that regular and pureed diet intakes were below 50% RDA in a female-only study, at 3.90±1.93 $\mu$ g and 3.28±1.28  $\mu$ g, respectively (50). These values are within the range of vitamin D intake seen with other EFR studies in this review. Overall, a slightly

wider range of EFR intake values were identified (0.7 to 7.05  $\mu$ g) (14,15,214,215,217–221) as compared to the WFR above. No clear speculations can be made regarding length of days recorded and vitamin D intake values, as a large range of intake values can be seen at the same length of intake recorded, especially for 3-day EFRs.

<u>Other:</u> A 1-day diet history done by Vikstedt et al. (Finland), noted lower vitamin D intake in females (6.6  $\mu$ g) than males (7.5  $\mu$ g) (222).

#### FOLATE

WFR: For folate, the 6 WFR originated from Austria, Canada, Spain, and Sweden, with length of WFR from 3-5 days. Sample size ranged from 30 to 252 participants. One study from Canada compared WFR and EFR to examine micronutrient intake, where WFR included meals only and EFR included meals and snacks (19). Both values were <50% RDA, but the WFR mean intake was lower (149±68 µg) than EFR mean intake (196±59 µg (male) and 161±78 µg (female)). The lowest intake (105.3±42.9 µg) was seen in Sturtzel's study (Austria) examining vitamin B6, B12 and folate intakes of LTC residents on laxative therapy (20). Folate intake values in these WFR studies ranged between 105.3 and 199 µg/d (19,210–213).

<u>EFR:</u> Two EFR studies examining folate intake originated from Denmark and the US. Sample size was 51 (50) and 104 (218) participants. The 1995 study by Johnson et al. (50) was female-only, used a 7-day EFR, and examined both regular and pureed diets. Residents on pureed diets were found to have lower folate intake ( $166\pm22 \mu g$ ) than those on regular diets ( $189\pm62 \mu g$ ) (47). The 2002 study was a 4-day EFR examining the relationship between added sugar consumption and nutrient density of Danish residents diets (218), where those with <10% energy from sugar had a mean folate intake at 197.1  $\mu g$ , those with10-20% energy from sugar a mean intake of 207.9  $\mu g$ , and those with  $\geq$ 20% energy from sugar had the lowest level of folate intake (151.8  $\mu g$ ). Overall the Beck 2002 study suggests that a high intake of added sugar in

residents' diets may lead to lower intake of micronutrients, and suggests the need for a nutrientdense diet. Number of days of EFR appears to not have had as great an influence on the mean intake for these two studies as compared to these other characteristics of the participants.

<u>Other:</u> The other citation identifying folate to be poorly consumed included 7-sites with a dietitian-administered FFQ where food grouping was used to identify food sources of riboflavin, folate and vitamin B12 (223). Folate intake was found to be  $187.3\pm81.1 \mu g$ , which fell within intake ranges seen in the WFR studies.

Six studies identified folate intake to be 50-99% RDA, originating from Australia (14), Canada (21), Finland (222), Spain (41,210), and the US (220). No studies identified folate intake to be >99% of the RDA. All but two of the five studies stating folate intake at 50-99% were conducted after 2000. The two studies conducted in the US before 2000 were conducted in 1982 (208) and 1996 (220), which was before mandatory folic acid fortification. Potential reasons for differences in intake may be due to geographic location and presence or absence of mandatory folic acid fortification policies, levels of folate in fortification, and the year the study was conducted (e.g. before or after implementation of fortification), and cultural food consumption patterns (e.g. high leafy green vegetables vs. high meat diets). Thus, despite fortification of folate, excessive intake in LTC are not a concern.

#### CALCIUM

<u>WFR:</u> Three studies examining calcium intake with WFR found intake to be <50% RDA. Length of WFR were at 5 (224), 7(212), and 21(5) days. Barr et al.(224) (Canada) examined intake of 30 female residents to determine the contribution of nutrients from different food groups, and found mean intake to be at 518.4 $\pm$ 210.4 mg (224). Wendland et al. (5) (Canada) investigated the intake of 23 cognitively impaired residents on regular and lactose-free diets, and

found calcium intake to be 458±140 mg on average. Moreira-Varela et al. (212) (Spain) examined 53 institutionalized residents and found calcium values to be 394±79 and 380±100 mg for males and females, respectively.

Conversely, more WFR studies cited calcium intake at 50-99% RDA (n= 8) than those that cited intake <50% RDA (n= 3). Calcium intake in these 8 studies ranged from 638 (225) to 910 mg (209). Cameron et al. identified the lowest calcium intake in the 50-99% RDA range with a 3-day WFR, and found that female residents had lower calcium intake ( $638\pm203$  mg) than males ( $812\pm309$  mg) (225). Lowik et al. identified the highest level of intake ( $910\pm430$  mg) with a 1-day WFR (209).

EFR: Two EFR studies noted low calcium intake. Length of these EFR were 1 (27) and 3 days (215) and sample sizes were 139 and 53 participants, respectively. For those without eating impairment, Nowson et al. (Australia) identified mean calcium intake to be at 406 mg (full diet), 286 mg (soft), and 292 mg (pureed); for those with eating impairments, calcium intakes were 310 mg, 376 mg, and 382 mg, respectively (45). Lee et al. (215) (Canada) assessed calcium and vitamin D status for diet alone and diet plus supplement, and identified lower calcium intake from diet alone for females ( $560\pm198$  mg) than males ( $847\pm264$  mg). However, with supplemental calcium at  $125\pm354$  (male) and  $384\pm533$ mg (female), total intakes were still below recommendations (total intake  $972\pm494$  and  $954\pm512$  mg, respectively) (43). Six EFR studies identified calcium intake between 50-99% RDA, with the lowest one just above 50% (600 mg) (19) and the highest one almost at the RDA (1080 mg) (218). Other studies fell between these ends of the spectrum, where a 7-day EFR by Johnson et al. (US) (50) found calcium intake at 660 mg for residents on a regular diet (667 mg for pureed diets), while another US study by Gloth et al. identified intake at 921 mg for sunlight-deprived residents (216).

<u>Other:</u> The last study citing a low calcium intake was an 11-site study using a 24-hour diet recall (226). They found average calcium intake to be 599.1±259.9 mg for female residents (226). In contrast, the highest level of calcium intake (>99% RDA) was also found in the Other category, where Vikstedt et al. found calcium intake to be 1247mg for males (1106 mg for females) with a 1-day diet history (222).

#### VITAMIN E

WFR: Two citations noting <50% RDA for vitamin E by WFR were recorded during a single 1.5 year longitudinal collection by Lammes et al. (Sweden) (211,213). Length of food intake data collection was 5 days (211,213) with 52 participants. Lammes' studies explored the relationship between energy and nutrient consumption of residents, and found that nutrient density was low for vitamin E, but that vitamin E intake increased with increased energy intake (intake mean of 4.8 mg (male) and 4.2 mg (female), and 4.6 mg (both genders) in the 2006 and 2009 studies, respectively). Lengyel et al. (Canada) also examined vitamin E with both a 3-day WFR and EFR with 48 participants (19). Interestingly, the WFR method found a higher vitamin E intake (7.9 $\pm$ 4.1 mg), and was the only study in this review to find vitamin E intakes between 50-99% of RDA. Yet, the EFR performed in this same study found lower vitamin E values where females consumed <50% RDA (6.4 $\pm$ 2.3 mg), but males consumed 50-99% RDA (10.2 $\pm$ 4.2 mg).

<u>EFR:</u> Two EFRs also noted low vitamin E intake, originating from Denmark and Canada. Length of data collection were 3 (21) and 4 days (218) with samples sizes of 407 and 104 participants respectively. As previously mentioned, Beck (Denmark) investigated the relationship between added sugar and micronutrient intake, and found an inverse relationship between added sugar and vitamin E status (mean intake: 3.56, 3.45, 2.58 mg at <10% energy from sugar, 10-20% and  $\geq$ 20%, respectively) (218). The second study was cross-sectional, and

examined residents from 11 LTC homes with normal nutritional status (93% had normal BMI). They found that 42.6% males and 52.8% females had a vitamin E intake below 50% of EAR (21).

<u>Other:</u> A 1-day diet history by Vikstedt (222) also found low intake in both female and male residents, 6.8 and 6.6 mg vitamin E, respectively.

# **Biomarkers of Nutrient Status**

In addition to food intake, micronutrient status can be assessed by biomarkers or biochemical measurements providing a snapshot of their levels or their activity in the body (e.g. PTH for vitamin D and calcium status). Biomarkers may be a more accurate method to determine potential micronutrient deficiency for some nutrients (39,40). Twenty-two studies were identified from the scoping review that contained biochemical data for residents' micronutrient status. The micronutrients examined are shown in Table 3. Studies were conducted between 1979 (56) and 2013 (227). The most frequently studied micronutrients using biomarkers were: vitamin D (n=11), calcium (n=7), iron (n=6), vitamin C (n=4) and vitamin B12 (n=5); other nutrients were vitamins A, E, B1, B2, B6, folate, chloride, copper, magnesium, phosphorus, potassium, selenium, and zinc. The micronutrients with low status using the AMA and/or CDC criteria were: vitamin D (4/11 and 8/11 citations using the AMA and CDC criteria respectively), vitamin C (3/5 per AMA and CDC), folate (1/4 per AMA, 0/4 per CDC), and iron (3/6 per AMA, no CDC cut-offs) (Table 3). However, AMA reference ranges and CDC cut-offs may differ from specific cut-offs used by the original articles, resulting in different counts of normal or low/deficient values. The differences can be seen in Table 3; specific reference values are available in Table 4. The potentially low status nutrients are discussed further below.

#### VITAMIN D

Vitamin D was assessed by two biomarkers, Serum 1,25-dihydroxyvitamin D (1,25(OH)<sub>2</sub>D) and 25-hydroxyvitamin D (25(OH)D) (Figure 3A) and the 11 studies were published between 1979 and 2011 (Table 3). Three studies measured 1,25(OH)<sub>2</sub>D status, and originated from Spain and the US (43,214,216) (Table 2). The study by Gloth et al. examined vitamin D status in sunlight-deprived residents confined indoors for 6 months or more, and identified the mean serum 1,25(OH)<sub>2</sub>D levels at 50.7(24.7) pmol/L (216). This was within normal cut-offs for CDC as well as Gloth's reference range, but low per AMA cut-offs. The other two studies using 1,25(OH)<sub>2</sub>D identified levels within AMA normal ranges.

All of these 11 studies measured serum 25(OH)D status: 2 identified vitamin D levels to be deficient (per CDC cut-offs), 6 identified low status (CDC cut-off), and 2 identified 25(OH)D status to be adequate (one study (56) stated low status but did not give numerical values). Studies examining 25(OH)D status originated from Australia, Canada, Ireland, the Netherlands, Norway, Spain, and the US. While Odowd et al. (1993) identified adequate 1,25(OH)<sub>2</sub>D levels, it also identified the lowest 25(OH)D status recorded in this scoping review, at 6.37 nmol/l (214). This study examined 109 residents from either a private nursing home or a US suburban public hospital LTC wing. Levels of both 1,25(OH)<sub>2</sub>D and 25(OH)D (36.2 nmol/L) were low for Gloth (216). For Perez-Llama et al, 1,25(OH)<sub>2</sub>D levels were adequate, but 25(OH)D levels were low for female residents (48.2 nmol/L) (43). The highest 25(OH)D status was identified by Johnson et al. (57), comparing vitamin D status between African American and White octogenarian and centenarians in the US. They found that, for those living in facilities, centenarians had lower mean 25(OH)D status than octogenarians, at 70.1 and 72.1 nmol/L, respectively. Yet both subgroups were above low cut-offs for AMA, CDC, and Johnson's references. Regarding gender differences, both Perez-Llama (43) and Woods (24) identified adequate 25(OH)D status for

males (53.4 and 51.5 nmol/L, respectively), but low statuses for females (48.2 and 38.0 nmol/L, respectively). Seasonal variations were addressed by Sem et al. (228), where mean serum 25(OH)D values were identified to be low for both winter and summer according to CDC and Sem's reference ranges (adequate per AMA).

#### VITAMIN C

Vitamin C was examined in five studies using four biomarkers (cell, leukocyte, plasma, and whole blood ascorbic acid) (Figure 3B). Studies were conducted between 1977 and 2003, and originated from Ireland, the Netherlands, New Zealand, and the UK (Table 3). Three of these five studies identified low plasma ascorbic acid (AA) values; other biomarkers for vitamin C were not found to be low. McClean et al. (229) examined the status of 35 male war veterans in New Zealand and identified mean plasma AA values of 16  $\mu$ mol/L. Marcenes et al. (49) assessed dental status of UK residents and found mean plasma AA levels of edentulous participants (1-10 teeth) to be low to borderline deficient at 11.4  $\mu$ mol/L (per CDC), while their dentulous (21 teeth or more) participants had adequate plasma AA levels of 31.0  $\mu$ mol/L. Vir et al. measured mean plasma AA status of residents in Ireland and found males to have deficient vitamin C levels (9.65  $\mu$ mol/L, per CDC cut-off), while females counterparts had adequate vitamin C status (23.3  $\mu$ mol/L, per AMA and CDC cut-offs) (56).

#### FOLATE

Four studies examined folate status using serum or plasma folate (Figure 3C). Studies were published between 1979 and 2010, and originated from Austria (20), Ireland (56), the Netherlands (54), and Spain (230) (Table 2). AMA identified one study with low plasma folate levels with residents on laxative therapy (20). However, using paper-specific cut-offs, a second study identified low plasma folate in older women in nursing homes with the Dutch Nutrition Surveillance System, where AMA had classified the values as normal (54). The remaining

studies assessed serum folate to be normal (56,230). These two studies included both genders, and assessed serum rather than plasma levels of folate.

#### IRON

Iron status was examined using six biomarkers: ferritin, hematocrit, hemoglobin, serum iron, total iron binding capacity, and transferrin (Figure 3D). The six studies were conducted between 1979 and 2013, and originated from Australia, Canada, Ireland, Italy, the Netherlands, and Spain. All biomarkers, with the exception of hemoglobin, noted normal iron status. Three of the four studies measuring mean hemoglobin levels identified low status, per AMA reference range. Lowik et al. reported low mean hemoglobin levels (13.4 g/dL) for 51 female nursing home residents in the Netherlands (54), while Vir et al. identified low hemoglobin values for males (13.9 g/dL) but adequate levels for females (14.3 g/dL) [Note: both values within normal cut-offs per Vir reference ranges] (56). Woods et al. examined 103 residents from 14 Australian facilities and reported low mean hemoglobin values for males and females, 13.2 and 12.7 g/dL, respectively [Note: both values within normal cut-offs per Woods reference ranges] (24). The one study identifying normal hemoglobin levels had values at the low end of normal (total 14.3g/dL; AMA normal = 14.0-17.5g/dL) (41).

#### 5.4 Discussion

The objective of this study was to identify and present a summary of micronutrients that are poorly consumed or at low biochemical levels for older adults in LTC. This is the first review, to our knowledge, to examine these issues for the LTC population. This study does not aim to determine the optimal micronutrient intake for older adults, but rather to assess micronutrient intake and biochemical status of LTC residents, to determine potential nutrients to target for intervention. The LTC population is diverse; some have cognitive issues, swallowing

difficulties, and varying amounts of health conditions, all of which may affect eating and nutritional status. Understandably, studies examining this heterogeneous population would be disparate, making it challenging to compare residents' nutritional intake and status.

# Overall Intake

This review identified several food intake studies with varied objectives, samples, and methods. Many factors are associated with micronutrient intake of LTC residents, and specifically in this review, diet texture (27,50), sugar consumption (218), sun exposure (216), laxative therapy (20), and dental status (49) were investigated. Regarding country of origin, most studies originated from Canada, Spain, and the US, and it appears that these countries have particular strengths in research for micronutrient intake in LTC. In this review studies were summarized by intake or biochemical data, and further classified by types of intake methods used (WFR, EFR, other), or by biomarker assessed. Calcium and vitamin D will be used to illustrate the various issues identified in this study with respect to addressing the purpose of this scoping review. Geographic differences and fortification practices affecting intake likely impacted the identification of low folate levels in this review, and these will be elaborated on below. The discrepancy between intake and biochemical data, potential gender differences and issues regarding choice of biomarkers and cut-off references will also be discussed.

# LENGTH OF DIETARY INTAKE ASSESSMENT, CHOICE OF SAMPLE AND OTHER ISSUES IN DIETARY ASSESSMENT: CALCIUM AND VITAMIN D AS EXAMPLES

From the 34 intake studies included, several assessment methods with differing lengths of diet intake assessment were used. Calcium intake had the widest range of days of intake measured, from a 1-day EFR to a 21-day WFR. Shorter studies provide less accurate information

on actual individual intake and patterns. For example, the number of days required for assessing specific nutrients for an individual has been suggested by Bingham (231), to be 10 days for calcium, 12 days for iron, and up to 36 days for vitamin C. Gibson has also identified preferred diet assessment approaches for various objectives (31). To determine mean nutrient intake of a group, a single 24-hour recall, WFR, or EFR from a large number of participants is required, while to determine the proportion of a population "at risk" would require repeated observations (31). Diet intake assessment methods (DIAMs) identified many micronutrients to be below DRI recommendations at 50-99% and some <50% of RDA. However, despite variety in the length of assessment, there generally was agreement among the types of DIAMS; for instance, micronutrients that were identified as low by WFRs were also identified as low by EFRs. Three day food records were the most common length of records performed. The largest 3-day WFR intake study of vitamin D and calcium was with 26 residents (56). The largest 3-day EFR intake study of vitamin D and calcium with a 3-day EFR with 169 residents (14). Both of these studies found vitamin D intake at <50% RDA (1.25±0.68 µg (Male)/1.07±0.39 µg (Female), and 1.78±2.05 µg for the WFR and EFR, respectively), and calcium intake at 50-99% RDA (892±81.8mg (Male)/ 868±142.7mg (Female), and 796±356 mg (total) respectively). While values were similar with these two studies, intake values vary with increasing length of intake examined, especially for vitamin D. A 4-day WFR found intake to be 3.90±4.64 µg  $(M)/2.49\pm1.15 \ \mu g$  (F) (43), a 5-day WFR identified  $4.5\pm1.4 \ \mu g$  (M)/ $3.5\pm1.3 \ \mu g$  (F) (211), and a 7-day WFR identified  $0.7\pm0.2 \ \mu g \ (M)/0.6\pm0.3 \ \mu g \ (F)$  vitamin D average intake levels (212). To note, the 7-day WFR study citing the lowest vitamin D intake was conducted in 1986 in Spain (second oldest vitamin D WFR study) (212). Although vitamin D fortification is not mandatory in Spain, there is increasing availability of vitamin D-fortified foods world-wide due to voluntary and mandatory food fortification, which may explain the higher vitamin D values seen in the

more recent studies (72,87,90,232). Alternatively, the more recent focus on adequate planning of diets for LTC with respect to this vitamin may have played into the higher intake seen in more recent studies. For EFR, the most common length was also 3 days; the largest variability was also seen with this length of assessment, as vitamin D intake ranged from  $0.7\pm0.2 \mu g$  (M)/ $0.6\pm0.3 \mu g$  (F) (n=109) (214) to  $7.05\pm3.65 \mu g$  (n=64) (216). These two studies were conducted in the US, in 1993 and 1995, respectively. Despite analyzing length of food record, sample size, and year of study, a clear trend cannot be identified to explain the variability in reported intake. This suggests the need for additional studies using longer food records and/or larger samples to improve the precision of population estimates and accuracy of individual intake data. It is noted that although some studies attempted to address the intra-individual variation in their determination of mean intake (e.g. Beck et al., 2002), many other studies did not.

Another issue in this research is the diversity in samples selected for inclusion and the focus of the original research question. For calcium, Barr et al. identified dairy products to be the highest contributor to calcium intake, but found an inverse relationship between dairy intake with age, although the relationship was not statistically significant (p=0.093) (224). Wendland et al. (2003) suggested that factors influencing micronutrient intake may be beyond actual intake, pointing to the sufficiency of food provision. In their study, they also included menu analysis investigating the intake of cognitively impaired residents on regular and lactose-free diets, finding that neither diet provided adequate calcium to meet recommendations. This was echoed by Lee et al. (2002), who found it unlikely that older adults could meet calcium and vitamin D recommendations from diet alone. Moreover, they found that diet plus supplement intake for both micronutrients also did not meet current RDAs for older adults. Changes in diet texture further complicates matters, as Nowson et al. (27) identified that calcium intake decreases as diet texture becomes downgraded. Also, those without eating impairment on a full diet had higher

calcium intake than those with eating impairments. The higher intake for eating impaired residents on soft and pureed is likely due to feeding assistance. All of this suggests that additional calcium provision, beyond what is provided by food alone, may be needed to meet residents' calcium (and other nutrient) recommendations, and specific subgroups of the population are likely at higher risk.

#### RESEARCH INTEREST: VITAMIN D AS AN EXAMPLE

Vitamin D was identified to be a micronutrient with intake <50% RDA by all DIAM (Table 3). As 19 of the 34 food intake studies examined vitamin D, it is apparent that research interest has been and remains high for this nutrient, providing greater information for this review than for any other micronutrient. For example, several studies examined vitamin D intake of pureed foods (Germain et al., 2006; Johnson et al., 1995; Nowson et al., 2003) providing more information for this vulnerable group than for other nutrients, which are also anticipated to be problematic. As well, we have identified of the source and timing of intake for vitamin D, but lack this information for other nutrients in this review. For instance, Johnson's study examined and specified vitamin D intake from meals, snacks, and nutrient supplements (50). Interestingly, the lowest vitamin D intake by WFR were identified by the oldest studies (1986 and 1979) conducted by Moreiras-Varela (212) and Vir (56), suggesting that potential changes in menu planning or supplementation have occurred over time with the known challenges with this nutrient.

This scoping review did not restrict the start date of relevant studies, providing an opportunity to demonstrate that research interest for some nutrients in LTC, like vitamin D, has always been high. The underlying assumption of research is that it is conducted in response to identified and/or evidenced need (233,234). For instance, with the Institute of Medicine's 2010

DRI updates for DRIs for vitamin D and calcium (235), the number of studies conducted around these two micronutrients in the following years also increased. Similar trends were seen for folate (236), vitamin C (237), and other micronutrients (238). Thus, research is also influenced by trending interests and available funding; the number of studies on a particular micronutrient does not necessarily imply its importance or potential for poor intake. Further examination of whether a broad spectrum of micronutrients are, in fact, poorly consumed is needed and this review has provided a starting point.

#### FOOD INTAKE VS. BIOCHEMCIAL ASSESSMENT

Despite numerous studies citing low (<RDA) micronutrient intake, when examining biochemical status, there were surprisingly few micronutrients outside of normal biomarker limits and only Vitamin D at low or deficiency cut-offs levels as per CDC references. Several reasons may account for these discrepancies. Certain studies used LTC staff to administer food records and collect data, while others had researchers or trained health professionals (e.g. dietitians); this may have affected the accuracy and consistency of intake data collected. For biochemical status, the dearth of studies using biochemical markers in LTC, and the appropriateness and adequacy of methods for assessing micronutrient status is problematic. With the exception of vitamin D, calcium, and iron, few studies have examined micronutrient biomarkers for older adults in LTC and only vitamin D and C showed consistency across most studies. Additionally, several different biomarkers were used, making comparisons across studies difficult, including lack of reference standardization between laboratories. Further, potential biomarkers for assessing micronutrient status are still being developed (40,47), and some existing biomarkers have limited usefulness due to tight self-regulation (e.g. serum calcium) or lack in sensitivity (e.g. decreases do not always indicate deficient states) or specificity (changes in response to more than one micronutrient status) (39,46). Moreover, there are discrepancies

between AMA reference ranges and CDC cut-offs, where AMA ranges are more often wider than CDC, resulting in overlap, as was seen with vitamin D. These discrepancies lead to difficulties in categorizing whether a micronutrient is within normal range, or at low or deficient values. For instance, if a study identified serum 25(OH)D level of 36 nmol/L, AMA would classify this as normal, while CDC would classify this as inadequate, leading to more inconsistency in categorization. Some studies on vitamin C (49,56,229), folate (20,54) and iron (24,54,56) also suggest a potential issue with adequacy, but there was no clear consensus between these studies; although levels were below normal, they were not low enough to be considered low/deficient by the original paper's cut-offs. The four micronutrients identified to be low based on biochemical assessment and the appropriateness of their biomarkers, according to EURRECA (39), are discussed below.

# APPROPRIATENESS OF BIOMARKERS USED FOR ASSESSING MICRONUTRIENT STATUS

The biomarkers used for vitamin D status were serum 25-hydroxyvitamin D (25(OH)D) and serum 1,25-dihydroxyvitamin D (1,25(OH)<sub>2</sub>D). According to the EURRECA Network of Excellence review, serum 25(OH)D is the most useful, robust, and reliable biomarker for assessing vitamin D status, as it reflects both dietary intake and skin synthesis for the vitamin (39). EURRECA found 1,25-dihydroxyvitamin D (1,25(OH)<sub>2</sub>D) to be not as useful as a biomarker for assessing status, as it is tightly self-regulated and reflects kidney function, rather than vitamin D status (39). Parathyroid Hormone (PTH) values were also not recommended as this parameter is not specific to vitamin D, but is also affected by calcium and phosphorus intake. Serum 25(OH)D was the most common biomarker used, and identified low vitamin D status in

the included studies, providing confidence in the conclusion that vitamin D is a nutrient of concern in this population.

Vitamin C status was assessed by cell, leukocyte, plasma, and whole blood ascorbic acid. Serum/plasma ascorbic acid is useful for measuring short-term intake status (fasting samples can reflect long-term status) (39). Leukocyte ascorbic acid is a sensitive biomarker, and is also better suited for measuring long-term vitamin C storage/status (39). Whole blood ascorbic acid is a less sensitive biomarker than the aforementioned (39). Plasma ascorbic acid was the most common biomarker used in the studies identified from this scoping review, and as it typically reflects short-term intake, it remains questionable if vitamin C status is truly low in this population. It was interesting to note that low vitamin C occurred in both older and more recent studies. Reasons for this may be due to lower intake of vegetables and fruits that provide vitamin C, as these foods may be more difficult to chew with age, and this factor has not changed in the population over time. This finding is supported by Marcenes et al. who identified residents with poorer dental status (fewer numbers of teeth) to have poorer vitamin C status compared to their dentate counterparts (49).

Plasma or serum folate are limited as biomarkers, as they only reflect recent intake (39). Homocysteine was reported by several studies, yet lacks specificity to folate, as it is also affected by B6 and B12, and was not used as a biomarker for this review. Sturtzel et al. examined residents on laxative therapy, and identified that these residents with low biochemcial values also had low folate intake (about 25% of DRI) (20). Lowik et al. examined older female nursing home residents and identified low plasma folate status along with low pyridoxal phosphate (PLP), 25(OH)D, ascorbic acid and selenium levels (54). Findings of low folate biomarkers were in agreement with a Norwegian study, outside of this scoping review, examining folate in nondisabled and disabled residents (239). Plasma/serum folate and PLP status were also found to

have a significant positive correlation (54). However, serum folate levels were within cut-offs for Huerta et al. (230), and Vir et al. (56). This lack of consistency across studies suggests that more work is needed to identify more accurate biomarkers, as current biomarkers have limited reliability (e.g. serum/plasma folate) and are overly influenced by recent dietary intake (39).

Iron status was measured by ferritin, hematocrit, hemoglobin, transferrin, serum iron, and total iron binding capacity (TIBC). Ferritin is the gold standard for measuring iron status (39). Hemoglobin measures anemia, and is a useful biomarker to measure changes in iron status with iron-interventions from a deficient state, yet it is not specific, as anemia may be caused by factors other than iron (39). Transferrin receptor measurements can be used to measure iron depletion, and is not affected by inflammation (39). TIBC can be used but lacks specificity, while serum iron is affected by diurnal variations, and both of these biomarkers should be used in combination with other biomarkers to improve interpretation (39). Hemoglobin was the only biomarker in this review to identify low iron status, but all three of these were borderline low-normal, ranging from 12.7 to 13.9 g/dL (24,54,56). These values are below the AMA cut-offs, but within normal limit of reference ranges used in all three studies (24,54,56). This suggests that iron status needs to be further investigated, as anemia can be caused by other factors such as chronic disease (240,241), especially in a LTC population.

# MICRONUTRIENT INTAKE AND BIOCHEMICAL STATUS: GEOGRAPHICAL AND GENDER DIFFERENCES

The heterogeneity of identified studies also included differences in geography. It has been noted that geographical differences may contribute to the variations seen in micronutrient status (242). Reasons for this may be due to diverse lifestyles, types of food consumed (243), fortification policies (73,90,244), and soil nutrients (245). This study addressed the potential

socio-geographic differences through exclusion of locations where lifestyle and diets may be less comparable (e.g. Asian countries) to the North American context. Moreover, with the LTC population, these differences may be minimized with regular provision and intake of meals, similar daily activities due to decreased mobility and increased functional dependency of residents (246). This is supported by this scoping review's findings, where intake data from much of the western world repeatedly cited similar micronutrients of concern. The question of whether these micronutrients affect health of older adults in LTC, regardless of location of residency, has yet to be answered. Moreover, relationships between LTC practice and residents' health status across different countries is still poorly-understood (4). Studies comparing international LTC homes agree that more focus is needed to address the increasingly complex needs of residents (4,246).

Of geographic interest are fortification practices, as these are different among countries. Mandatory fortification programs were implemented in 1998 for Canada and the US, and in 2009 for Australia (247). The seven studies that identified folate intake <50% RDA were from Austria, Canada, Denmark, Spain, Sweden, and the US (247). The US study was done in 1995 (before mandatory fortification)(50), and may explain the low folate intake found. However, the Canadian study that found low folate intake was done in 2008 (19), suggesting mandatory fortification practices may not completely address micronutrient needs in LTC, at least in Canada. The 6 studies identifying 50-99% folate intake originated from Australia (14), Canada (21), Finland (222), Spain (41,210), and the US (220). The Australian and US studies were done before implementation of fortification, in 2007 and 1998, respectively. However, the Canadian study was done in 2007, and also found low (50-99%) folate intake, reiterating the above finding that fortification of grains may be inadequate in Canada to meet the RDA for this population.

Regarding gender, while most studies included both genders, several intake studies were female-only (50,54,224,248) (Table 2), while several biomarker studies were female-only (54,249), and one was male-only (229) (Table 3). Studies have shown that females in LTC traditionally have lower biochemical status compared to males (250,251). Yet, it is unknown whether gender differences in micronutrient intake and biochemical status are due to intrinsic physiological differences (252), culturally-based (253), or simply due to different food preferences and foods consumed (254), including the amount of energy. Gender differences did not show a consistent trend in this scoping review, in that certain biochemical or intake studies found lower values for females (18,24,43), while others found higher (56). Overall findings of micronutrient intake and biochemical status from gender-specific studies in this review were generally within those ranges of studies that included both genders. More work is needed to examine both genders so that potential differences can be further examined.

# 5.5 Limitations

This first scoping review on food intake and biochemical micronutrient status in LTC has several strengths, including a comprehensive review of the literature and reliability checking of extracted data. Yet there are limitations. Specifically, intake and biochemical status data were separately reviewed, and we cannot comment on the adequacy of diet to attain biomarker levels within normal ranges. Due to the heterogeneous methods of the included studies, sorting by intake and biochemical data was the most logical method to present the data. However, several studies examined both intake and biochemistry. This is beneficial, as a true understanding of potential deficiency requires examination of both aspects as well as functional markers of the nutrient (31).

Additionally, comparison of biochemical data between studies was difficult due to the lack of standardization between labs including: diverse lab kits, analysis methods, assays, and reference values used. As noted in this review, values may be considered normal by one reference and low by another. This was addressed by comparing biomarker results to both reference values from the original studies, along with AMA to provide a standard comparison, and CDC cut-offs to determine level of inadequacy if values which were well below normal levels. As well, this study cannot comment on the adequacy of nutrient intake for functional outcomes, including the health of residents. Lastly, this paper only identified vitamin D as low or deficient using biochemical analysis. Yet, low dietary intake (<50% RDA and 50-99% of RDA) was identified by many different studies for several nutrients. This incongruence suggests that further work, especially linking food intake to functional outcomes in LTC is needed, as intake can be below the RDA, but still meet the individual's requirement. The ultimate goal of identifying micronutrients of concern for older adults is to strengthen our understanding of how micronutrients enhance health outcomes for older adults. First, the relationship between micronutrient intake and potential status should be demonstrated through use of selected biomarkers. Next, the relationship between biochemical status and specific health outcome must be shown. This study provides a foundation and reference for micronutrients of concern for LTC by presenting residents' intake and biochemical status. Future work is needed to demonstrate the connection between planned diets, micronutrient intake and health outcomes.

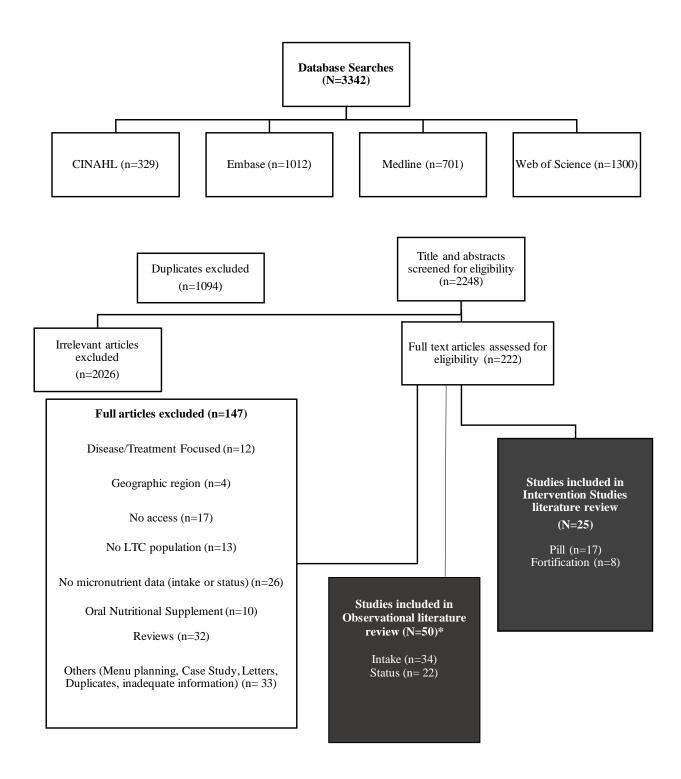
# 5.6 Conclusion

This scoping review examined LTC residents' micronutrient intake and biochemical status. The micronutrients that were most concerning due to low intake were: Vitamin D, folate calcium, and vitamin E. The micronutrients that were most troubling according to biochemical status were: vitamin D, C, folate, and iron. Intervention strategies, such as fortified foods or

supplementation could be considered if dietary intake alone is unable to meet needs, especially for vitamin D where consistency was seen in food intake and biomarker assessment. With the growing number of residents in LTC, along with their increasingly complex health needs, it is an opportune time for research and testing of interventions to meet potentially insufficient intakes.

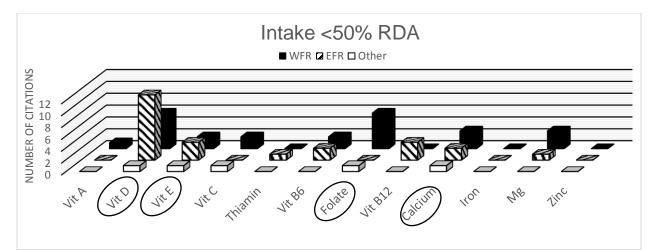
#### **Take-Away Points**

- Micronutrient intake of LTC residents is affected by many factors, including diet texture sugar consumption, sun exposure, laxative use, and dental status
- Intake is below the RDA for many micronutrients; vitamin D, folate, calcium, and vitamin E had intakes consistently below 50% of the RDA (or the EAR) and are the highest priority for interventions
- Micronutrients identified to be below normal limits via biochemical assessment were: vitamin D, C, folate, and iron; only vitamin D was sufficiently low to be considered deficient
- Biochemical status is difficult to compare due to lack of inter-laboratory standardization
- Future studies should combine multiple methods (e.g. menu analysis, intake assessment, biochemical assessment) to adequately examine the complex nutritional status of the LTC population

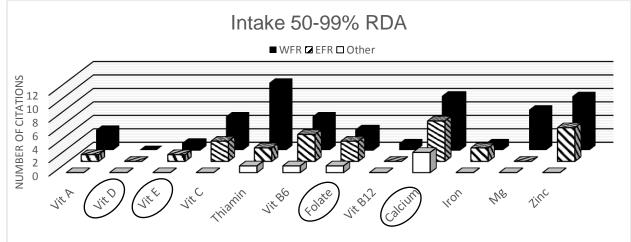


**Figure 1**. Flow diagram of study (N= number of studies)

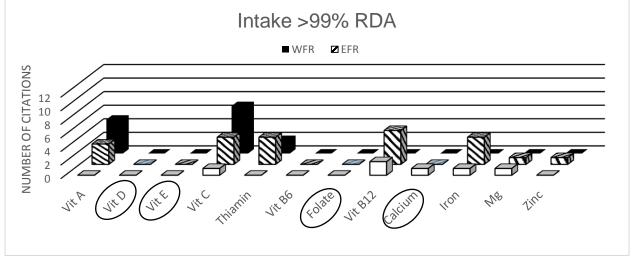
\*Number of intake and status studies overlap; Final results are in the black box



**Figure 2A.** Dietary Intake Data. Comparison of commonly cited micronutrients by Dietary Intake Assessment Method (DIAM) at <50% RDA. Circled=4 micronutrients with lowest intake.



**Figure 2B.** Comparison by Dietary Intake Assessment Method (DIAM) at 50-99% RDA; AI is used for Copper, Pantothenic acid, Potassium (< AI)



**Figure 2C.** Comparison by Dietary Intake Assessment Method (DIAM) at >99% RDA; AI is used for Copper, Pantothenic acid, Potassium (>AI)

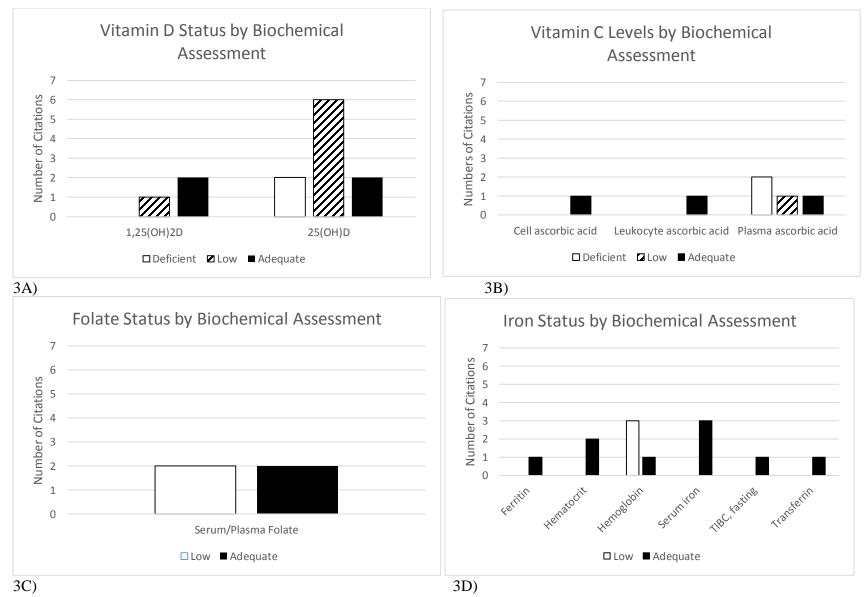


Figure 3. Micronutrients of Concern by Biochemical Assessment Methods

# Chapter 6

# Scoping Review: Pill Supplementation and Food Fortification in Long-Term Care

# (A Scoping Review on Micronutrient Supplementation and Fortification Intervention

#### Studies)

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#### Abstract

Micronutrient deficiency is a prevalent yet preventable form of malnutrition among long-term care (LTC) residents, negatively affecting their functional abilities, cognition, and quality of life. Adequate intake of a varied diet is needed to meet micronutrient requirements, but physiological factors including eating difficulties, taste changes, and decreased appetite often hinder residents' food intake. Micronutrient fortification and supplementation are strategies to promote nutrient intake. This scoping review was designed to map the health literature to determine: 1) the efficacy of micronutrient supplementation, and 2) food fortification in LTC. Using the scoping review framework of Arksey and O'Malley, a comprehensive search strategy of four electronic databases (MEDLINE, EMBASE, CINAHL, and Web of Science) was completed. Preliminary results found 2248 relevant articles for abstract and potentially full article review. Application of inclusion/exclusion criteria resulted in 25 relevant studies: 17 pill-form studies and 8 fortification studies. Overall, vitamin D (n=17 citations) and calcium (n=12) were the most common micronutrients to be included in both pill supplementation and food fortification formulations. Vitamin C (n=8), folic acid (n=7), and zinc (n=5) were also commonly included in formulations. In conclusion, the scoping review methodology allowed for mapping and categorization of a disparate literature related to micronutrient interventions in the LTC setting. The preliminary findings suggest a need for: 1) trials comparing the efficacy of single-micronutrient and multimicronutrient formulations for both supplementation and food fortification in the LTC population, and 2) studies comparing the efficacy between supplementation and food fortification with the same micronutrient formulations.

Key Words Micronutrient; Food Fortification; Supplementation; Long-Term Care

#### 6.1 Introduction

Long-term care (LTC) homes or facilities are a growing option for medical and custodial care for older adults in North America (255–258). Numerous factors diminish the LTC population's ability to meet their nutrient needs, including: chronic or acute disease, malabsorption, depression, decreased appetite, and low food intake, resulting in malnutrition. Protein energy malnutrition (PEM) is commonly described (108,202,259,260), but micronutrients are also known to play a role in optimizing or maintaining health of older adults (67,74,261,262) and poor intake and micronutrient malnutrition is a documented issue in LTC (5,21,263,264). At present, there is no consensus on the best way to treat micronutrient malnutrition in LTC residents (26).

Oral Nutritional Supplements (ONS) are commonly prescribed for LTC residents with low food and fluid intake to address PEM (107), or to improve overall clinical outcome (265). Formulations high in protein, protein and calories, and/or with specific micronutrients to address chronic disease (e.g. wound healing) are available (107). Compliance with provision and acceptance, especially in residents who require assistance to eat, is the greatest challenge with this strategy (266). Suboptimal intake and high wastage of ONS has been well-documented (267,268), with dislike of flavour, texture, or taste being the most common cause for refusal (268,269). Research suggests that families (270) and providers (108,271) prefer a 'food first' approach in addressing nutritional problems, especially as ONS may replace food intake (272,273). As ONS are often only introduced when a significant nutrition problem is noted, they are not preventative (271). For those with limited weight loss but poor intake, ONS may result in unnecessary weight gain and is not a first-line approach for addressing potential micronutrient

problems. Thus, alternative, longer term strategies to address potential micronutrient inadequacies should be considered (273–275).

Oral vitamin/mineral pills are used in LTC to address micronutrient needs for specific or overall nutrient inadequacies (276,277). This method allows for individualized nutrient provision for residents. However, not all oral vitamin/mineral supplements are covered by drug benefit plans, potentially thus incurring higher administrative costs for the LTC home or the resident (119,278). Residents may also refuse pills due to swallowing difficulties, or have low adherence for pill supplementation when it is crushed and provided in food due to the unpleasant taste. Studies have demonstrated the efficacy of micronutrient supplementation in addition to food when dietary intake is inadequate to meet physiological needs, especially for pregnant women (279), infants (280), adolescents (281-283), and disease states (284), yet there is less literature examining the efficacy of this strategy for the LTC population. There is some resistance with increasing medications of any type in this environment; attending physicians have been shown to view such supplements as extra medication, and have been known to refuse certain vitamin and mineral orders due to lack of clear benefits (285). Lastly, there is the risk of drug-nutrient interactions when administering vitamin/mineral pills at the same time as medications meant to be taken without food (29), which renders this choice less desirable. Neither of the two previous strategies are 'food first' approaches for increasing residents' nutrient intake and require intervention and behaviour modification by staff and the resident.

Enriched/fortified foods have been proposed as a 'food first' approach to addressing nutritional issues and improving health status (107,108), requiring no change in behaviour on the part of the resident. Creative methods have been used, but the focus is usually on protein and energy with the addition of milk, eggs, or cheese added to selected foods (107). Liquid or

powdered protein supplements are also available to be added to the diet (108). While these strategies appear to improve energy and protein intake (109), these enhanced foods typically do not focus on improving micronutrient intake (107). Fortification has been considered a potential solution to micronutrient malnutrition in the elderly population (29,110), but there is no consensus on which micronutrients to include in formulations, at what dosage, and in which food vehicles (food to which micronutrients will be added).

Certain micronutrients in fortified or supplemental form may also be more bioavailable than natural food-form (e.g. vitamin B12), and may be particularly beneficial for older adults with absorptive issues (e.g. atrophic gastritis)(Russell, 2001) and fortified or supplemental sources of food have been recommended for older adults (28). Due to the differences in bioavailability, the upper limit for certain micronutrients (e.g. vitamin E, niacin) only apply to supplements or fortified foods, but not natural food form (28). Little is known about the risks and benefits of micronutrients in both supplemental and fortified forms for the LTC population. Pills and fortification are both options to enhance micronutrient intake, but their efficacy is not fully understood. As it was unclear if there was sufficient evidence to support a systematic review using a focused question, a scoping review to map this literature was undertaken. The primary purpose of this study was to explore the evidence on micronutrient-focused interventions in LTC, specifically pill and food fortification strategies, to determine the range of micronutrients studied, the dosages and length of treatment, and the efficacy of these approaches, to determine gaps that need to be addressed with further research. A secondary purpose was to identify which nutrients and foods could successfully be used for food fortification.

#### 6.2 Method of Review

A scoping review was the chosen method for this literature review. This method provides an opportunity to quickly explore a body of literature, allows for summary and dissemination of research findings, and helps identify research gaps in existing literature when the research conducted to date in a specific area is diverse (124). Scoping reviews have been recommended for areas of research that have yet to be reviewed in a thorough manner (141). The five stages of a scoping review have been detailed by Levac et al. (2010) using the Arksey and O'Malley framework (124,142). Compared to a systematic review, scoping reviews allow reviewers the ability to address broader topics (124), especially when the question is less focused, helping to map out relevant literature in the field of interest (144) including grey literature (124). Thus, the flexibility of a scoping review is well-suited to the exploratory nature of this study.

In order to enhance the rigor and comprehensiveness of the search, key search terms related to: 1) micronutrient deficiencies, and 2) micronutrient food fortification that were specific to the LTC population were identified and reconfirmed with a health research librarian as well as co-authors. The search included four diverse databases: Ovid MEDLINE, Ovid EMBASE, EBSCO CINAHL, and Web of Science. Searches were iterative, and terms were changed, refined and finalized to ensure a comprehensive search. No date restrictions were used to allow for broader inclusion, with December 31<sup>st</sup>, 2012 as the last publication date. Key articles were hand-searched for further citations. This broad search strategy captured both observational and intervention studies, and was later divided as two papers to allow more in-depth descriptions of each type of study. This paper will only discuss results of the intervention studies.

Inclusion and exclusion criteria were applied to all titles and abstracts. Citations had to be intervention studies that included, at minimum, results of the effects of one or more

micronutrients in pill or food-form for a LTC sample. For studies examining multiple participant groups (e.g. community, retirement and LTC participants), only results specific to LTC residents were included and if results were merged across sectors, the citation was excluded. Studies using ONS were also excluded, as these provide macronutrients as well as micronutrients, and effects of micronutrients alone cannot be ascertained. Citations with food intake data and/or biomarkers assessing status were included, and were limited to the English language. Studies conducted in North America, Europe, Mediterranean (Greece, Italy, Portugal Spain) and Scandinavian countries (Denmark, Finland, Iceland, Norway, Sweden), New Zealand, and Australia were included; differences in foods consumed, LTC nutrition care processes, and micronutrients of interest in other geographic regions were anticipated and thus studies from other regions excluded. The initial screening process of titles, abstracts and where required full text, was conducted by the first author (IL) with agreement with the senior author (HK). A subsequent title and abstract review process was completed by a second trained reviewer using the same inclusion/exclusion criteria in efforts to avoid missing key articles from the search results. Any articles in question to be included in the review were examined by the senior author and both authors came to a decision on inclusion or exclusion. Pertinent information was extracted to a spreadsheet, and 100% of the articles were divided and reviewed among the authors to validate this extraction.

#### Data Extraction, Categorization, and Synthesis

A flowchart of the number of studies examined and included is found in Figure 1. Data extracted included participant characteristics (age (mean ± standard deviation), study design (sample size, length of study, intervention type, dosage), assessment methods (biomarkers used),

and changes identified in outcome variables for both intervention and control groups, if available. Studies were divided into two categories, depending on whether the intervention was delivered in pill-form or food form.

#### 6.3 Results

The search strategy resulted in 3342 articles in total (Figure 1). Full articles initially selected for inclusion were excluded if they: focused on disease/treatment (n=11), were not part of the geographic region for inclusion (n=4), the full citation was not accessible (n=12), did not include a LTC population (n=13), did not present micronutrient data (intake or biochemical) (n=26), focused on the use of oral nutritional supplements (n=10), were reviews and not original studies (n=32), or did not address our research question (e.g., menu planning, letters to the editor, had outcome measures other than biomarkers (e.g. falls, infections), enhanced foods by ingredients rather than micronutrients for fortification (e.g. trialing fortified infant cereal as a thickener to add nutrients to thickened foods) (n=25). The screening criteria resulted in 25 intervention studies, with 17 studies trialing micronutrient pills and 8 testing food fortification. Results from pill-form studies will be presented first, then food fortification data (Tables 5A to 8A for change in biomarker status (increase/decrease), Tables 5B to 8B for actual/numerical values). As the majority of interventions trialed vitamin D and/or calcium, these two micronutrients were sorted into one subgroup for both pill- and food-form, and all other micronutrients were put into a second subgroup for discussion.

## **Comparison to Dietary Reference Intake and Biomarker Reference Values**

A variety of efficacy end points (e.g. prevention of fracture with vitamin D) were used in the studies identified. As our primary research questions were focused on micronutrient status and due to these various functional end-points used in studies, efficacy in this review is defined as achieving normal serum levels of the selected biomarkers for individual nutrients. Dosage levels for supplementation and fortification were compared to the Institute of Medicine's Recommended Dietary Allowance (RDA), which provides a reference to meet nutrient requirements for nearly all (97-98%) individuals in a particular gender and age group (e.g. those >70 years old) (28). Micronutrient intake was compared to the RDAs for individuals greater than 70 years of age to allow for standardization of resulting data, as other nations may follow their own version of dietary references (28). Adequate Intake (AI) was used if RDAs have not been established for a particular micronutrient. Recommendations for males were used if recommendation levels for the genders varied (See Table 9-12C for comparisons to RDAs).

As citations used a variety of biomarkers with varying reference ranges, to promote comparison across studies, the American Medical Association (AMA)'s reference ranges, which are commonly used in both scientific and medical settings, were used (44). Since AMA provided values for normal ranges, values from the Centers for Disease Control and Prevention (CDC) (45) were also included to provide reference ranges for values that were below normal (low and deficient values).

The two most common micronutrients included in intervention (supplementation and fortification) studies were vitamin D (n=17 citations) and calcium (n=12). Vitamin C (n=8), folic acid (n=7), B12 (n=6), B1 (n=6) and zinc (n=5) were also commonly included in formulations.

The efficacy of supplementation or fortification with these micronutrients will be discussed below.

#### **Pill-Form**

## Vitamin D and Calcium

This scoping review identified 9 citations trialing vitamin D and/or calcium in pill-form (Table 5A). Studies in this category originated from Brazil (286,287), Canada (94), France (288,289), Ireland (290), The Netherlands (105), Norway (99), and Switzerland (291). Studies were conducted between 1987 (288) and 2011 (290). Randomized controlled trial (RCT) was the most common design (n=5), with length of study ranging from 4.5 months (105) to 2 years (99,291). RCT sample size ranged from fifty-six (287) to 3270 residents (289). The remaining four studies were a pre-test/post-test with one (286) or two comparison groups (290), and post-test studies with a comparison group (288) or the intervention group only (94). Length of study for these non-RCTs ranged from 12 weeks (286,290) to 10 months (94) and sample size ranged from forty-two (286) to 104 residents (288). The biomarkers used to assess vitamin D and calcium status were: 1,25(OH)D, 25(OH)D, calcium (ionized and total), parathyroid hormone (PTH), phosphorus, osteocalcin, and alkaline phosphatase. Vitamin 25(OH)D was the only biomarker that was used across all studies.

**Dosage trialed compared to RDA:** The RDA for vitamin D and calcium are 800 IU and 1200 mg per day, respectively. There were three vitamin D-only studies (94,99,286), and six included both vitamin D and calcium (Table 5A) (105,287–291). Three studies considered factors that could affect the efficacy of supplementation (e.g. body fat, dose timing/schedule) (105,286,290). The dose of calcium in all but one study were below the RDA (27-83% RDA) (105,287,288,290,291). One study supplemented with calcium at 100% RDA (289). A wider

range of dosage was seen with vitamin D, where values ranged from 50% to 306% RDA. Three of the 9 vitamin D studies had values at the RDA (288–290), 4 were above the RDA (94,286,287,291), and only one was below the RDA (75% RDA) (105). None of the studies had values above the Tolerable Upper Intake Level (UL).

Seven studies used daily vitamin D dosage schedules, providing 400 IU (99) to 2000 IU (94) vitamin D per day (Table 5A). Two studies examined weekly dosages of 4200 IU (105) and 7000 IU (286) per week, and two studies trialed monthly doses at 18000 IU (105) and 150000 IU (287). Of the six studies that included calcium, dosage ranged from 320 mg (105) to 1200 mg (289) in elemental form. For change in biomarker status, this review will only examine 25(OH)D, calcium, and PTH status, as these were common across all studies in this category.

**Biomarkers compared to AMA and CDC Cutoffs:** For vitamin D, all studies achieved normal 25(OH)D status according to the AMA reference ranges (35 – 150 nmol/L) (44) and CDC cut-offs (50-70 nmol/L for 25(OH)D sufficiency) (45), regardless of dose or length of study. Although there may be a positive dose-response, larger number of studies would be needed to clarify any dose-response trend of vitamin D, and likewise for other micronutrients.

*25(OH)D:* All studies found an increase in 25(OH)D status. Dinizulu et al. identified the greatest 25(OH)D increase (61 nmol/L from baseline) with 800 IU/day vitamin D (100% RDA) alone for 12 weeks.(290) This study also tested 800 IU/day vitamin D with 1000 mg/day calcium (83% RDA) and found a smaller increase (37 nmol/L) with the combined intervention, suggesting that a single vitamin D intervention may be as effective as a combined calcium-vitamin D intervention for improving serum vitamin D status (290). Schwalfenberg et al. supplemented 2000 IU/day vitamin D (167% RDA) for an average of 8 months and noted an increase of 4-4.2 nmol/L for every 100 units of vitamin D given (based on 35-40 nmol/L).

25(OH)D at baseline) (94). The smallest increase (17 nmol/L) was found by Meyer et al., trialing only 400 IU/day of vitamin D for 2 years (99).

*Calcium:* The six supplementation studies that included calcium with vitamin D reported final serum calcium status (total and/or ionized) in all intervention groups to be above the AMA reference ranges (no CDC cut-offs available) (105,287–291). Concern with calcium supplementation and increased risk of adverse cardiovascular events (292–294) will be further elaborated on in the overview section below. All participants had calcium status within normal ranges at baseline. Moreover, two studies found decreased calcium status from baseline (287,291), yet final values were still within AMA normal ranges. Krieg et al. supplemented residents with 880 IU vitamin D (110% RDA) and 500 mg elemental calcium (42% RDA), but found a small decrease in calcium for the treatment group (2.32 to 2.31 mmol/L, baseline to final) and an even larger decrease for their control group (2.29 to 2.23 mmol/L) (291). Moreira-Pfrimer et al. trialed 150,000 IU per month for 2 months and 90,000 IU vitamin D per month for 4 months (~3667 IU, 306% RDA) and also identified a decrease in ionized calcium for both the treatment (1.3 to 1.25 mmol/L, baseline to final) and the control groups (1.3 to 1.27 mmol/L) (287). However, total calcium increased for their treatment group (2.23 to 2.27 mmol/L), but decreased in their control group (2.25 to 2.23 mmol/L) (287).

Dinizulu et al. trialed a vitamin D-and calcium and a vitamin D-only formulation, and identified the largest increase in calcium (0.1 mmol/L from baseline) with the combined vitamin D and calcium formulation for 12 weeks (290). The vitamin D-only formulations showed a smaller increase in calcium status (290). Further, Meyer et al.'s vitamin-D only formulation with 400 IU/day (50% RDA) also showed the lowest and non-significant increase in serum calcium (0.003 mmol/L) (99).

*PTH:* Parathyroid hormone status was examined in eight of the nine studies and a decrease was found in six citations (286–291). Chapuy et al.'s 1987 study found the largest decrease of intact PTH (60.3 ng/L, baseline to final) in a 6 month intervention of 800 IU vitamin D (100% RDA) and calcium (1000 mg, 83% RDA) (288). This is contrasted with the control group, which found an increase of 18.2 ng/L. Dinizulu et al.'s vitamin D, with or without calcium intervention, identified the next largest decrease in PTH, (40 ng/L with calcium, 30 ng/L without calcium) (290).

#### Other (Non-Vitamin D/Calcium) micronutrients: Zinc, vitamin C, vitamin E

Eight citations trialing other (non-vitamin D and calcium) micronutrients in pill-form were identified. Five were multi-nutrients (95,98,205,295,296) and 3 were single-nutrients (100,158,297). Studies were conducted between 1993 (95) and 2011 (297). The dosage content and levels used in the multi-nutrient studies were heterogeneous, and no clear trends could be identified. Overall, zinc was the most common micronutrient assessed with multi-nutrient supplementation (n=5 citations), followed by vitamin C and E (n=4 each). Vitamin D was also part of formulations (n=3), but not calcium. (See Figures 4A and 4B for comparisons of dosage trialed vs. RDA for vitamin D/Calcium, and other micronutrients, respectively.)

For the five multi-nutrient interventions, biomarkers examined were vitamins A, D, E, C, B6, B12, thiamin, riboflavin, and folate, copper, iron (ferritin), selenium, and zinc. These studies originated from Australia (295), France (95,296), the UK (98), and the US (205) (Table 6A). All were RCT designs with study length ranging from 1 month (95) to 1 year (205), and sample size ranging from eighty-four (95) to 617 residents (205). Four studies supplemented zinc in

combination with other micronutrients (98,205,295,296), with dosage ranging from six (295) to 20 mg (296) elemental zinc.

For single-nutrient studies, biomarkers examined were vitamins C, B12, iron (hematocrit, mean corpuscular volume), and zinc. Studies originated from the Netherlands (100), Switzerland (297), and Turkey (158). Two RCT studies were conducted (100,297), and the other design was a pre-test/post-test (158).

**Dosage trialed compared to RDA recommendations:** Large variations in dosage were trialed in the multi-nutrient studies (e.g. vitamin C dosage ranged from 30 to 200 mg (30 to 222% RDA), vitamin E ranged from 6.8 to 90 mg (45 to 606% RDA), zinc ranged from 6 to 20 mg (55 to 182% RDA)) (Table 6B, Figure 4B). In all five of the multi-nutrient studies, and in two of the three single-nutrient studies, some micronutrients were above the RDA; there was no consistency among which nutrients were supplemented above this reference value. Two studies had values at or above the UL; Grieger et al. supplemented with 313% RDA (50 mg) for niacin in a multi-nutrient formula to improve nutritional status and bone quality (295), and Meydani et al. supplemented a multi-nutrient formula with 500% RDA vitamin D (4000 IU) with the intended purpose of reducing instances of respiratory infection (205).

## Biomarkers compared to AMA and CDC Cutoffs:

<u>Multi-nutrient results:</u> Allsup et al. tested a multi-nutrient formula (Vitamins: A, D, E, B1, B2, B3, B5, B6, B7, folic acid, B12, C; Ca, Cu, Fe, I, Mg, Se, Zn; see Table 10C for dosage levels) with 119 residents (n=61, treatment) receiving influenza vaccines for 8 weeks. They identified a significant increase in levels of vitamins A, D, E, C, folate, and selenium from baseline (98). Levels of vitamin D and C for the treatment group were below AMA normal ranges at baseline but improved to normal ranges with fortification. Zinc levels remained below

AMA at baseline and finals. Levels of the remaining micronutrients were within AMA normal ranges at baseline and final. Interestingly, the dosage levels of all micronutrients in Allsup's study with the exception of vitamin D, were above the RDA for nutrients. The authors did not record changes in vitamin B12 despite high dose given. Asciutti-Moura et al. examined a vitamin-only intervention (Vitamin E, C, B1, B2, B3, B5, B6) with 84 residents (n=27, treatment) for 30 days, and found a significant increase in serum vitamin C (ascorbate), vitamin E (males only), and erythrocyte thiamin pyrophosphate (95). However, levels of riboflavin and vitamin B6 decreased (95). Final levels of vitamin C and E remained within AMA normal ranges; no AMA comparisons were available for the biomarkers used for thiamin, riboflavin and vitamin B6. Grieger et al. trialed a multi-nutrient formulation (vitamins A, D, E, C, thiamin, riboflavin, niacin, pantothenic acid, B6, B7, Folic acid, B12; Ca, Fe, Mg, Mn, K, Zn) for 24 weeks with 92 residents (n= 49, treatment), and identified a significant increase in 25(OH)D (27.4 nmol/L), folate (13.0 nmol/L), and vitamin B12 (145.6 pmol/L) (295). Levels of zinc decreased by 0.1 µmol/L, but was not found to be significant (295). This formulation was adequate to help maintain folate and B12's AMA cut-offs for adequacy (both were normal at baseline as well); despite the decrease, average zinc level was still within AMA cut-offs. However, vitamin D remained below AMA normal ranges. Yet, proportions of participants at low levels of 25(OH)D ( $\leq$ 50 nmol/L), folate ( $\leq$  7 nmol/L), and vitamin B12 ( $\leq$ 200 pmol/L) also decreased from 37% to 23%, 14% to 0%, and 30% to 6%, respectively (295). Meydani et al. focused on the effects of a vitamin E on respiratory infections in 617 residents (n=311, treatment) for 1 year, and combined vitamin E (90 mg, 606% RDA) with 50% RDA for vitamins and minerals (Vitamins A, D, C, B1, B2, B3, B6, Folic acid, B12; Cu, Fe, I, Se, Zn) in the intervention group compared to a control without vitamin E (only 50% RDA of other vitamins

and minerals) (205). A significant increase of plasma vitamin E was found in the intervention group (26.5 to 49.2 µmol/L, baseline to final; both baseline and final levels were above normal ranges), yet there was no significant change in other micronutrients' statuses (205). Monget et al. examined the effects of a vitamin-only (Vitamins A, E, C); and a vitamin-and-mineral-combined intervention (same vitamin content with Se and Zn added), with 575 residents for 6 months (296). All dosages were at or above the RDA, and a significant increase in serum B-carotene (vitamin A), a-tocopherol (vitamin E) and vitamin C were seen in the vitamins-only group; a significant increase in selenium was found in the minerals-only and the combined vitamin-and-minerals groups (baseline values were below AMA; final values reached AMA normal ranges with fortification); and a significant increase in zinc was seen in the minerals-only group (final value still below AMA normal ranges) (296).

Single-nutrient results: Favrat et al. trialed vitamin B12 at 1000  $\mu$ g for 4 weeks with 50 residents (n=26, treatment), and found a significant increase of B12 (101.6 pmol/L) as compared to the control (297). Levels of B12 were maintained within AMA normal ranges for both treatment and control groups, but a smaller increase was seen in the control group. A significant decrease in methylmalonic acid levels was also found (0.13  $\mu$ mol/L, p<0.001), yet homocysteine levels also increased (but was non-significant, p=0050). Ter Riet et al. trialed vitamin C at 1000 mg for 12 weeks with 88 residents (n=43, treatment) and identified an increase in plasma ascorbic acid levels (64.2  $\mu$ mol/L, no p-value given) (100). Both treatment and control groups' final values were within AMA ranges, but a smaller change was seen in the control group. Finally, Arcasoy et al.'s pre-test/post-test intervention study trialed zinc supplementation at 30 mg for 90 days with 15 residents, and found an increase in serum levels (12.96 to 14.34  $\mu$ mol/L, baseline to final; both baseline and final values were within AMA normal ranges) (158).

## Biomarkers compared to AMA and CDC cut-offs: Vitamin C and zinc as examples

*Vitamin C:* All five multi-nutrient supplementation studies included vitamin C in the formula, but only three measured vitamin C status (95,98,296). One vitamin C single-nutrient supplementation study also supplemented with calcium (100). Overall, all of these studies that included an outcome of vitamin C status showed an increase from baseline to final with the intervention. Three supplementation studies had residents with vitamin C levels below AMA and CDC cutoffs at baseline (98,100,296), while one had normal baseline values (95). While means of average values post intervention were in the normal range, large standard deviations were also seen (98,296). Thus, individual participants' final vitamin C values may still be below cut-points for normal.

*Zinc:* Three of the five pill studies increased zinc levels with supplementation sufficiently to meet the AMA cutoffs (98,158,296), while the other two studies found that zinc status decreased (205,295). The three studies with final values that met AMA cutoffs for zinc also had within normal values at baseline, so the efficacy of treatment is questioned for improving zinc status.

#### **Food Fortification**

#### Vitamin D and Calcium

Vitamin D with calcium were trialed by four food-fortification studies (Table 7A). Three studies in this category originated from France by Bonjour et al. (111,115,298); the other originated from Romania (112). Studies were conducted between 2009 (112,115) and 2013

(298). Food vehicles included cheese (111,115), yogurt (298), and buns (112). Dosage schedules provided 100 IU (111,115) to 5000 IU (112) vitamin D per day (Table 7A) and elemental calcium at 280 mg (298) to 320 mg (112) per day. RCTs were used by two studies with a sample size of twenty-one (111) and 59 residents (298), and length of study of 6 and 8 weeks, respectively. The other two studies used a pre-test/post-test one group design with the length of study being one month (n=35 residents) (115) and one year (n=45 residents) (112). Across all studies, biomarkers used to assess vitamin D and calcium status included: 25(OH)D, calcium (serum and urine), parathyroid hormone (PTH), phosphorus, osteocalcin, and alkaline phosphatase. For change in biomarker status, this review will only examine 25(OH)D, calcium, and PTH status.

**Dosage trialed compared to RDA recommendations:** Three of the four studies were conducted by Bonjour et al., and aimed to reduce bone resorption markers or decrease bone loss; they trialed formulations that were below the RDA for both vitamin D and calcium with dairy products (cheese and yogurt) as the vehicles (111,115,298). Range of dose in these studies were from 13-50% RDA for vitamin D, and 25-67% RDA for calcium. Mocanu et al.'s study trialed the safety and efficacy of a pharmacological dose (above the UL) of vitamin D (5000 IU, 625% RDA) in a bun (112). The accompanying dose of calcium was 302 mg (27% RDA) (Table 11C).

#### **Biomarkers compared to AMA and CDC Cutoffs:**

Overall, from the combined observational and intervention studies scoping review there were many more studies using dietary assessment methods (Figure 5A) compared to biomarker measurements (Figure 5B). 25(OH)D: 25(OH)D status increased for all four intervention studies. The largest increase was seen in Mocanu et al.'s one-year trial of a bun with 5000 IU/day

vitamin D (625% RDA) and 320 mg/day calcium (27% RDA), where 25(OH)D status increased from 28.8±9.9 nmol/L (baseline) to 126.4±37.3 nmol/L (final) (112). Bonjour's trialing of cheese with 100 IU/day (13% RDA) vitamin D and 302 mg/day calcium (25% RDA) also identified increases in serum 25(OH)D after 1 month (32 nmol/L from baseline) (115), and 6 weeks (~7.5 nmol/L from baseline) (111). This study had a high compliance rate of 93.4%. The next largest increase (25.3 nmol/L compared to control) was Bonjour et al.'s 2013 study, trialing yogurt with a 400 IU vitamin D (50% RDA), and 800 mg calcium (67% RDA) (298). This study had 89% adherence. The other two studies found smaller increases of 25(OH)D status and did not provide data on compliance rates (112,115). For these fortification studies, all but one study (115) achieved normal 25(OH)D status per AMA reference ranges. Using the CDC cut-offs, two studies did not achieve 25(OH)D sufficiency (115,298). The 25(OH)D outcome level in Bonjour et al.'s 2009 study (115) where the intervention group did not meet AMA or CDC cut-offs did show a significant increase from baseline (baseline): 13.73(4.24) nmol/L; final: 15.72(4.24) nmol/L). Reasons for this may be the low dosage (100 IU/day), and the short intervention duration (1 month) (115). It has been estimated that 3 months are needed to achieve steady levels of 25(OH)D status with vitamin D supplementation (299,300) and fortification is anticipated to have at least this or a greater time requirement for achieving normal vitamin D status. A larger increase in 25(OH)D was found in Bonjour's 2013 study, which met the AMA criterion, but not CDC (298). This study had a higher dose (400 IU), but it was still lower compared to supplementation studies (94,112,286), and length of the intervention was just under two months. Only one study was conducted for over 2 months; Mocanu's study was the longest vitamin D and calcium study and was conducted for 1 year (112).

*Calcium:* Three of the four studies examined serum calcium status. Bonjour's 2013 study trialing yogurt found that levels did not significantly change from baseline to follow-up, however, the control group in this study showed a non-significant decrease at follow-up (298). The calcium decrease in the control group was also not statistically significant. The remaining two studies were pre-test/post-test studies with one group only; as with the RCT, both identified small, non-significant decreases in serum calcium levels from baseline to final (112,115). Bonjour (2009) saw decreased serum calcium with fortified cheese (2.29 to 2.27 mmol/L) (115) and Mocanu identified decreased levels with use of fortified buns (2.29 to 2.28 mmol/L) (112). Yet, average calcium values for participants were within the AMA normal range at baseline and final. This suggests that the calcium dosage provided may be too small or fortification intake occurred at too short of a duration. However, this may also be due to the homeostatic control of serum calcium. Mocanu also measured urinary calcium and a slight increase was seen (3.4 to 3.7 mmol/L, baseline to final), indicating that increased calcium absorption (and excretion) occurred at this dose (302 mg calcium), without evidence of hypercalcemia (112). For Bonjour (2009), despite the non-significant decrease in serum calcium, there was an improvement seen in other bone resorption markers (e.g. PTH) suggesting some benefit of fortification of foods with calcium at these < RDA levels (115).

*PTH:* Parathyroid hormone status was measured by all four studies, and found to consistently decrease with treatment. Mocanu et al. reported the largest decrease in PTH, from 59.3 to 19.0 ng/L (baseline to final) and Bonjour (2013) found a similar decrease (28.6 ng/L, baseline to final) with their yogurt fortification (400 IU vitamin D and 800 mg calcium for 56 days) (298). Bonjour's other two studies trialed cheese (100 IU vitamin D and 302 mg calcium)

with a 1 month pretest/post-test study with 1 group and 6 week RCT crossover, and found a decrease of 9.2 ng/L(115)(Bonjour et al., 2009) and ~3ng/L (111), respectively.

#### Other (Non-Vitamin D/Calcium) Micronutrients:

Four studies trialed food fortification with other micronutrients (Table 8A). Studies originated from Canada (119), Ireland (117), the Netherlands (301), and Spain (116). Studies were conducted in 1995 (301), 1998 (117), and 2009 (116,119). Food vehicles included juice (301), milk (117), margarine (116), and pureed entrées (meat and vegetable portions) (119). Folic acid was trialed in all four studies. Other micronutrients in these formulations were: Vitamins D, E, C, thiamin, riboflavin, niacin, pantothenic acid, B6, biotin, folate, and B12. Interestingly, none of the formulations in this category included minerals. Aims of these studies included improvement of folate status (116,117), reducing malnutrition (119), and examining the effects of increasing micronutrients on nutritional status (96).

**Dosage trialed compared to RDA recommendations:** Three studies provided micronutrient dosages below the RDA (116,301). However, one study by Adolphe et al. fortified with levels at or above the RDA for all nutrients, except for vitamin D (80% of RDA) (119). Two studies were folic acid-only (116,117), and two were multi-nutrient studies that included folic acid (119,301). Ranges were from 16-100% RDA (Table 12C). Bermejo et al. conducted a pre-test/post-test study with a treatment and comparison group (n=126 residents) trialing folic acid-fortified margarine (200  $\mu$ g/10 g margarine, 50% RDA) for 6 months, and identified an increase of serum and erythrocyte folate, from 16.6 to 27.1 nmol/L (baseline to final) and 748 to 1403 nmol/L, respectively (116). This group also estimated that the remaining 200  $\mu$ g of folate would come from food, thus achieving the 400  $\mu$ g folate recommendations. Keane et al.

conducted a post-test 2-group comparison only study with 89 residents (n=49, treatment) trialing folic acid-fortified milk for 6 months at 76  $\mu$ g/day (19% RDA) and identified a significantly higher level of serum folate in the treatment compared to the control group, at 5.81  $\mu$ g/L and 2.16  $\mu$ g/L, respectively (117). Red blood cell folate was also higher in the treatment compared to the control group, at 316.5  $\mu$ g/L and 196.1  $\mu$ g/L, respectively (117). Keane et al. concluded that folic acid fortified milk was an acceptable and effective method in administering folic acid to LTC residents (117).

Van der Wielen et al.'s (1995) RCT trialed a water-soluble vitamin-fortified juice (vitamins C, B1, B6, folic acid, and zinc) with 33 residents (n=15, treatment) for 12 weeks, and Adolphe et al. used a pre-test/post-test design with one group (n=11 residents) trialing a vitaminonly formulation (Vitamins D, C, B1, B2, B3, B5, B7, folic acid, and B12) in pureed vegetable and meats for 8 weeks.

#### **Biomarkers compared to AMA and CDC Cutoffs:**

Vitamin C: Only one fortification study examined vitamin C level; levels for the treatment group was with the normal range per AMA and CDC at baseline and final, and the control group's baseline was below normal (301). In this study, significant increase of plasma vitamin C was seen in the treatment (2.4  $\mu$ mol/L) and control (0.9  $\mu$ mol/L) groups with fortification.

Folic Acid: All four studies had final folate levels within normal ranges for AMA and CDC references. Folate levels increased for three of the four studies (119,301); one study did not measure baseline values (117). However, baseline values for the studies where provided were also within AMA and CDC normal ranges.

Others: Results from Van der Wielen's (1995) study identified a significant increase in thiamin (+17 nmol/L from baseline) and vitamin B6 (+16 nmol/L), and significant decrease in serum homocysteine levels (-7  $\mu$ mol/L) in the treatment group (301). Adolphe's study identified a significant increase in 25(OH)D and folate status, but did not find a significant increase in vitamin B12 status (119).

# 6.4 Discussion

The primary purpose of this review was to examine the available research on pill and fortified food forms of micronutrient delivery for LTC residents and specifically to identify the range of micronutrients examined, the range of dosage used, and the resulting effects. The secondary purpose was to determine which nutrients and foods have been successfully trialed and incorporated for food fortification. Research to date favours a pill-based strategy over food fortification to promote micronutrient intake of older adults in LTC. However, most of the fortification studies were conducted in the past decade (111,112,115,116,119,298), suggesting an increasing interest in this strategy. Overall, improvements in blood nutrient makers were seen with both fortification and supplementation, with many reaching AMA and CDC cut-points to indicate sufficiency, yet heterogeneity in study design, intervention length, dosage formulation (single or combined), dosage schedule, and foods trialed make comparisons difficult.

## **Overview of Effects of Micronutrient Supplementation and Fortification**

## Dosage Recommendations

Several challenges arose in comparing and interpreting the findings in these identified studies, specifically considering the doses provided in formulations. Overall, it appears that both

pill and fortified food forms of micronutrients are effective at improving micronutrient levels, yet it is unknown whether doses delivered in supplements or in food are equivalent in terms of efficacy; as well most supplements in reviewed studies were well above the RDA while fortification studies were at or below the RDA, except for the study by Adolphe et al. (2009).

The updated DRIs consider older adults (>70 years of age), and included data from actual studies rather than simple extrapolation from younger adults (302). However, these are set for healthy individuals; the multi-morbid resident in LTC may require different nutrient recommendations due to different nutrient requirements in disease states and possible changes in metabolism of nutrients (263,302,303).

Besides the DRI, other recommendations have been suggested regarding intake and supplemental levels of micronutrients. For instance, Osteoporosis Canada has provided more elaboration to the current calcium RDA due to recent research suggesting an association between calcium supplementation and risk of adverse cardiovascular events (292–294), recommending that the 1200 mg should come mainly from food rather than from supplements/fortification (304). However, this same advocacy group recommends vitamin D intake for older adults to go above the RDA, suggesting an intake of 800-2000 IU/day vitamin D (100 – 250% RDA), which is the level shown to increase serum 25(OH)D to desirable levels (305). In reviewed studies where vitamin D was provided at 800 IU or higher (112,290,291), larger increases in 25(OH)D were seen as compared to dosages below the RDA (98,99,115). The Linus Pauling Institute (LPI) also suggests targets for micronutrient intake for older adults (65), taking into consideration decreased appetite, absorption changes (e.g. atrophic gastritis), and body stores. LPI also recommends 2000 IU/day vitamin D from supplements due to decreased ability of skin synthesis of vitamin D for older adults (65). Other recommendations for older adults from LPI

include supplementation of 400 mg/day vitamin C at minimum due to heightened needs from chronic disease, protective benefits of vitamin C against oxidative damage, and possible decreased ability to use vitamin C with age (65,306). Hence, when considering supplementation or fortification dosage, it is important to examine older adult-specific recommendations to target levels based on their specific needs.

#### Dosage and Efficacy

In this comparison of studies, AMA and CDC were used to determine potential efficacy of dosages. Although many studies demonstrated final levels within these reference ranges, many baseline values are also considered normal. It needs to be noted that dosage levels reported in these studies may not have been high enough to meet functional outcomes, especially as in some studies that included functional or health-related outcomes, benefits were often not seen.

#### Factors affecting non-response

In particular, minimal change was seen in calcium levels despite a wide range of dosage given (25-100% RDA), where all calcium studies had values within AMA range, whether an increase or decrease was identified. This is not surprising, as the body maintains circulating calcium levels for physiological reasons, and serum levels are thus not reflective of bone mineral content (39,307). The decreases in serum calcium seen in these studies may point to potential issues with nutrient metabolism and excretion for older adults due to declining renal function with age (302). Ionized calcium is the active form of calcium and may better reflect functional status, but levels are affected by age and other factors (39). There are currently no reliable biomarkers to assess change in calcium status from interventions due to tight homeostatic

regulation, making assessment of status difficult (39). Thus, non-response may be due to insensitive biomarkers to measure changes with intake levels. Future studies with calcium in LTC need to examine other outcome measures to demonstrate potential benefits of supplementation or fortification.

For micronutrients where change was not found with supplementation or fortification, it is important to examine whether this is due to high levels of micronutrients at baseline, low dosage or short duration of micronutrient interventions, as was demonstrated by the vitamin D fortification example above. Asciutti-Moura et al. conducted a study with vitamins E, C, thiamin, niacin, and B6, and found that while levels of vitamin C and E increased, B6, thiamin, and riboflavin remained the same (95). This lack of change in status of these micronutrients may not only indicate that doses were too low, but also that there may be a greater need for these micronutrients for LTC residents (95).

#### Concerns with Toxicity and Overconsumption of Micronutrients

The Tolerable Upper Intake Levels (UL) has been established to determine the highest level of long-term intake for individuals without presenting adverse health effects (28,37). Individuals at higher risk of toxicity would be those who consume large amounts of high nutrient foods, select a higher proportion of fortified foods, or who take supplements as well as fortified foods (37). Given the commonly low food intake in LTC (5,21), and pre-portioned foods at mealtimes, it is less likely that LTC residents will overdose on fortified foods from excessive consumption of said fortified food. However, more work will be needed to determine the maximum portions that individuals can have of the fortified food, should they request additional amounts. Ideal single and double (triple, etc.) portions and their micronutrient content should be calculated to ensure that the total amount provided of fortified foods does not exceed the RDA or approach the UL. The full RDA or AI should also be divided amongst servings, and not be provided in one serving, for this reason. This would also counter the problem of a refused food and then the missed opportunity for fortification.

The most commonly trailed micronutrients were vitamin D, calcium, vitamin C, folic acid, and zinc. Remarkably, many supplement studies had dosage above the RDA or AI, yet only two studies had levels above the UL (112,295); neither of these studies reported adverse effects. This could indicate that older adults in LTC require levels above the RDA for certain micronutrients to maintain health status or avoid decline, or alternatively length of follow-up of studies was insufficient to see adverse events.

#### **Delivery Methods of Micronutrients**

## Pill Supplementation vs. Food Fortification

Studies have compared the bioavailability of supplemental vs. natural/food-forms of micronutrients (308–310), yet this review did not capture any studies that compared the effects and differences between pill-form or fortified food-form of delivery of micronutrients to LTC residents. Other than calcium, none of the fortification studies in this review trialed minerals. Adolphe et al. initially trialed pureed entrées with minerals, but decided to use a vitamin-only formulation to avoid taste-issues with the fortified food (119). Regarding dosages in food, with the exception of Mocanu's (2009) study, dosages were generally below RDA levels, rather than pharmacological levels of nutrients. One reason for this may be due to taste changes in foods with the addition of micronutrients (119), or differences in regulations between fortified foods and pills (89). Thus, due to the differences in dosages between fortification and

supplementation, where supplementation can more easily reach pharmacological levels, it is difficult to compare the effects of these two strategies.

Although there were more supplementation studies than fortification, the lack of consistency in formulations (different micronutrients were trialed at various doses) and study length makes comparisons within supplementation studies challenging. For instance, for vitamin D doses ranged from 400 IU per day for a 2-year intervention to 150,000 IU per month for a 6-month intervention. Thus, even when only one micronutrient is compared, the variability in formulation and intervention length may not allow for an easy comparison. This becomes more difficult for multi-nutrient formulations.

For fortification studies, differences in formulations and food vehicles for the limited studies, also makes comparisons and conclusions on their effect difficult. One study compared natural food-form and fortified food forms of folate, using vegetables and fortified margarine, and found that, while both methods increased folate status, there was lower compliance with vegetable intake, and fortified margarine was a well-accepted and more effective method to increase folate status in LTC residents (116). Thus, food preference alone may render one fortification strategy more effective than another due to better acceptance. Further, it illustrates the importance of selecting food vehicles that residents enjoy, to increase the likelihood that targeted intake levels will be achieved.

**Challenges with Supplementation:** Micronutrient supplementation is a simple and direct method in delivering micronutrients, and does not depend on the resident's appetite. However, compounds in pill-form are not all equally effective. One study examining the intestinal absorption of magnesium from food vs. supplement and found that foods high in magnesium are as bioavailable as supplemental forms of soluble magnesium acetate, and that

enteric-coated magnesium chloride had much lower bioavailability than magnesium acetate (310). Thus, it would be important to determine the compound with the highest efficacy. Further, the level of micronutrient that could be added in supplemental form may be limited by the size of the pill. For instance, multivitamin/mineral pills generally do not contain the RDA for calcium as the pill would be too large if all 1200mg calcium were incorporated. Lastly, polypharmacy continues to be a challenge for older adults in LTC and other settings (58,102,103,311). Use of nutrient supplementation has been discouraged without good clinical evidence of benefits to avoid adding additional stress and burden with medication consumption for older adults (58,312). Concurrent use of medication with micronutrient supplementation may increase adverse side effects (104,312).

**Challenges with Food Fortification:** Outside of the LTC context, other studies have examined bioavailability of food fortification and pill supplementation (37,302,313,314). Compared to pills, food fortification has the additional challenge of identifying a food vehicle that enhances rather than inhibits the absorption of a nutrient (315). Simply adding nutrients to a food may render the nutrient unavailable if it was added to a product with many inhibitors of said nutrient, such as iron and phytates (77). However, addition of micronutrients to food via fortification may be beneficial as certain nutrients enhance absorption of other nutrients (e.g. iron and vitamin C) (77). One study outside of the LTC sector, compared absorption of folic acid-fortified cereal-grains (bread, rice, pasta) and supplements, and found fortified forms to be highly bioavailable for improving folate status and was comparable to supplemental form (309). Colman et al. studied folate-fortified staple foods, where folate levels increased with both folic acid-fortified maize and rice products, but lower absorption levels were found with fortified bread (308). Two cooking methods (boiling and baking) were contrasted, with baking for longer

time found to be more damaging to folic acid levels. Hence, careful selection of food carriers and cooking methods is required and when comparing products, examination of bioavailability is needed (308).

Besides calcium, none of the fortification studies included minerals in the formulation. Adolphe et al. suggested that the minerals may alter the taste and colors of foods it is incorporated into (119). Hence, stronger tasting and darker color foods may be needed to mask the changes caused by the addition of fortificants. In addition to determining the micronutrients of greatest risk of deficiency, future research should also identify commonly consumed foods in LTC and trial fortification formulations with these foods to assess whether it is possible to add these nutrients without changing the color, texture, and taste of the food.

#### Single or Multi-Micronutrient Delivery

Micronutrients were provided in single, dual (e.g. vitamin D and calcium) and multiple nutrient formulas for both supplementation and fortification. While single micronutrient delivery could more clearly demonstrate the effects of a particular micronutrient, there is also value in providing micronutrients in combination as some micronutrients enhance the absorption of others. It is not known whether providing multiple nutrients in a formulation may attenuate the effects of a single nutrient (65). However, it is known that certain micronutrients require other micronutrients to work optimally (e.g. calcium and vitamin D) and appears to be an approach consistent with natural food consumption. Meydani et al. trialed vitamin E with other micronutrients, contrasted with just the other micronutrients alone at a low dose; they found that only vitamin E levels increased (205). The addition of other micronutrients in the control group may have improved the overall nutritional status of residents in the control group, thus

potentially reducing the effects of vitamin E alone. Yet doses were too small to show a significant increase in biomarkers of these other nutrients (205).

# **Choice of food vehicle for Food Fortification**

The foods trialed in fortification studies can be classified as beverages (milk (117) and juice (301)), condiments (margarine (116)), sides (bun (112)), snacks (cheese (111,115), yogurt (298)), and entrées (pureed meats and vegetables (119)). Similarities between these foods are that they are commonly found in LTC and are available to different diet types and textures or can be easily modified (e.g. pureed foods for dysphagia). Certain food vehicles also originally contained lower levels of the micronutrient, but were still considered sources of these nutrients (e.g. cheese and yogurt for calcium and vitamin D). Yet above all, these studies indicate that whichever food vehicle is selected for fortification, it must be well-accepted by residents for an effective intervention and feasible to put in more than one portion per day.

## **Biological Significance of Findings**

In addition to nutrient biomarkers, other outcome measures were also measured, such as respiratory infections (205), pressure ulcers (100), fractures (99), and bone quality (111,115,295,298). This scoping review presented change in micronutrient status as the outcome measure as this is specific to micronutrients, and is the anticipated immediate result of supplementation or fortification, yet it does not allow for clarification on the functional effects of these micronutrients. This is of interest, as it has been shown that food fortification is able to improve nutritional but not functional status of residents with respect to frailty (316). However, biomarker sensitivity is still an issue. For instance, assessment of calcium status from serum

biomarkers is difficult, as calcium is tightly regulated in the body, which may render it less sensitive to changes in intake and status (39). Thus, identification of appropriate, specific and sensitive biomarkers is much needed in both research and practice. This review captured statistical significance of supplementation or fortification of micronutrients, and also determined whether certain dose, formulation, and length of supplementation reached normalcy regarding micronutrient status cut-offs, but still cannot determine whether a certain dose of micronutrient is biologically or functionally significant (e.g. reduction of morbidity and mortality), as would be the ultimate goal of delivering micronutrients to older adults in LTC. Several studies demonstrated that both fortification and supplementation were able to improve micronutrient levels to meet AMA or CDC cutoffs, decreasing the risk of deficiency and subsequent negative health outcomes. It has been suggested that change in micronutrient status may be affected by the baseline level of biomarkers, where a greater response to the intervention may be seen in those with lower levels at baseline (112). Given that older adults in LTC commonly have poor nutritional status, they may be more likely to benefit. Long-term clinical consequences of increasing vitamin and mineral levels are still unknown (95) and future research in this area is needed, but identification of more accurate and reliable biomarkers can help to better assess older adults' micronutrient status and status and functional changes with interventions (39).

## 6.6 Strengths, Limitations and Future Work

A strength of this study was that it was not limited to a specific functional outcome, such as respiratory infections (205), hip fractures (288,291), pressure ulcers (100), or simply to avoid/correct deficiency levels (116,117,158,297) ensuring that a maximal number of studies were included for comparison. The effects of a wide range of dosages was also examined.

Despite the heterogeneous outcome measures, by selecting changes in micronutrient status, this scoping review was able to compare the results from these diverse studies.

Advances in Fortification: From this study, there appears to be an increasing number of fortification in recent years (112,116,119,298). Reasons for this include increased interest in optimal health, and changes in the purpose of fortification, where efforts are no longer restricted to addressing population-wide deficiencies, but rather towards voluntary fortification such that industry can choose to fortify certain foods with certain micronutrients in order to promote health (90). Both research and regulations are still in progress for voluntary fortification (317,318).

Supplementation vs. Fortification: At this point, it is difficult to determine whether fortification or supplementation is a better strategy to improve micronutrient status of older adults, especially of multi-nutrient formulations. To fully answer whether micronutrient-fortified food or supplemental forms of nutrients are more efficacious, a better understanding of micronutrient bioavailability, metabolism and excretion in older adults is needed (261). It is currently unknown whether the bioavailability of micronutrients are different in pill-form vs. fortified food form, and whether the absorption or excretion rates may require different micronutrient cutoff points to determine normalcy for older adults. Clear benefits of vitamin D and calcium in pill form were seen in this review, but comparable dosage levels were not seen in fortification studies. The purpose of fortification, which is to provide micronutrients for the whole LTC population, compared to supplementation, which is a more targeted intervention for individuals, suggests that both strategies could be beneficial in LTC to meet micronutrient needs. As poor nutritional status and likely poor intake of micronutrients is common in LTC (24,227,319), micronutrient fortification may be an effective strategy in addressing micronutrient needs of the wider LTC population. This may also help reduce polypharmacy (58,103,312), and

promote quality of life by providing a "food first" approach that is more enjoyable for residents (320).

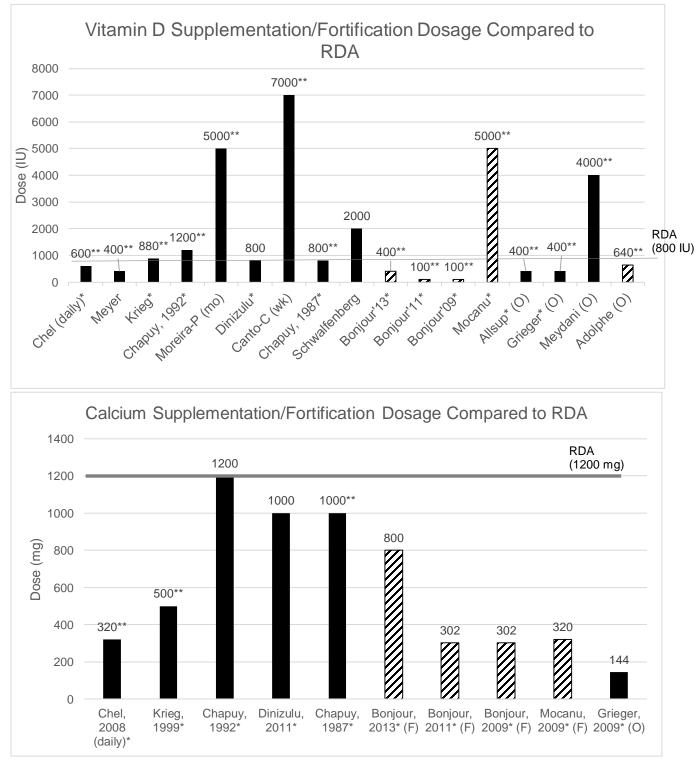
Study Limitations: Limitations of this study revolve around the dearth of available reference ranges available for micronutrients and the variation in the studies identified. As the AMA reference ranges did not include all micronutrients examined in the identified studies, or did not include the biomarkers used in the studies, not all micronutrients could be compared to AMA to determine whether levels were within normal ranges, affecting overall interpretation of this work. The heterogeneity of data in the studies identified, as well as the lack of appropriate biomarkers were limitations to the accuracy of the study. This study also did not examine compliance of treatment, as not all studies provided this information, yet compliance would undoubtedly affect treatment outcomes. Changes in micronutrient statuses were examined, but overall intake was not examined, and a direct relationship between intake and status cannot be made from this study, yet this is needed to demonstrate the efficacy of micronutrient-enhancing strategies.

**Future research:** Future studies should determine whether there are benefits to providing fortified food compared to pills and to determine whether incorporation of micronutrients into foods enhances or inhibits absorption of micronutrients. Long term clinical consequences of vitamin and mineral supplementation or fortification should also be examined. The greatest challenges with this type of study will be the limits of dosage in the food form due to potential taste changes. Single vs. multi-micronutrient formulations should also be trialed, to examine whether there are benefits to providing nutrients in combination with each other, or whether nutrients may interact with competing effects. It is also important to compare and determine the bioavailability of different forms of micronutrients, to determine which form of

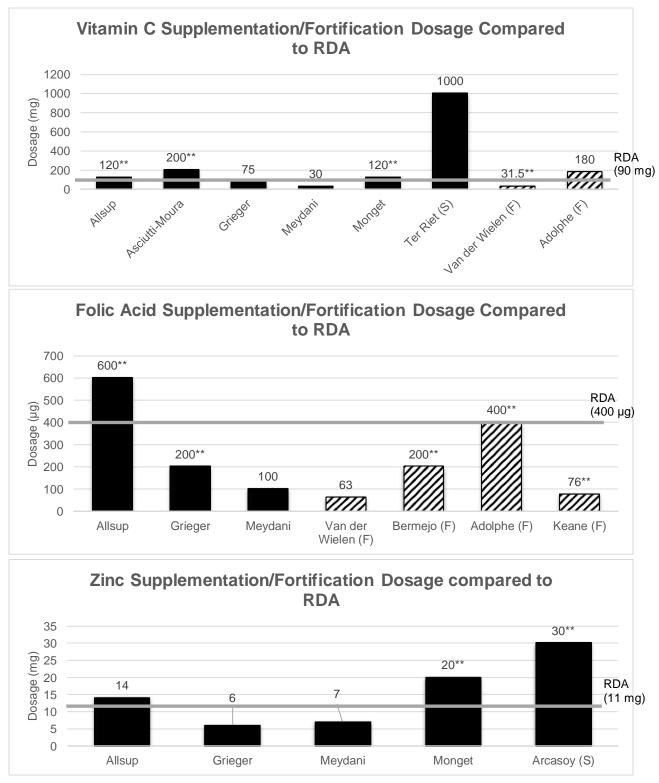
micronutrient to add to the fortification formula. Care must be taken with the food vehicle, not only to allow for better bioavailability of nutrients, but also to ensure residents will accept and completely consume the food vehicle for proper delivery of micronutrients. Focus groups with LTC staff and residents to determine preferred and commonly consumed foods are recommended to achieve this objective and to better understand the LTC context and potential issues with food fortification in LTC. For recommendations to LTC practice, in addition to adding nutrients to foods, proper food preparation procedures are also necessary to enhance micronutrient content of provided foods. A better understanding of how to enhance bioavailability of food with different cooking practice or food-processing practice may be an effective strategy to improve micronutrient intake before implementation of fortified foods (321).

# 6.6 Conclusion

In conclusion, addition of micronutrients via fortification appears to be a feasible alternative to current micronutrient delivery methods, and may be as effective as pill-form delivery of micronutrients for improving residents' micronutrient status, at least when using AMA and CDC cut-offs as the criterion. Given the low levels of food intake and poor health status of residents (5,21), and the low biochemical levels of certain micronutrients, strategies to improve micronutrient status are needed; supplements certainly work, but more research is needed on fortification. Vitamin D is likely beneficial for inclusion into a fortification formula due to decreased sun exposure and poor nutrient absorption of LTC residents absorption (285), but controversial findings of other micronutrients (e.g. vitamin C, folate, zinc) warrant future studies. More work is also needed to identify appropriate food vehicles for fortification that not only enhance bioavailability of micronutrients, but are also well-accepted by residents.



**Figure 4A. Micronutrients assessed by biomarkers in Calcium/Vit D interventions** \*Formulations contains vitamin D with calcium, (F) Fortification studies, (O) Formulation contains vitamin D and calcium with other micronutrients, \*\*Sig. increase in status with supplementation/fortification (25(OH)D for Vit D, serum Ca for calcium)



**Figure 4B. Micronutrients assessed by biomarkers in non-Calcium/Vit D interventions** (F) Fortification studies, (S) Single-nutrient study, \*\*Sig. increase in status with supplementation/fortification

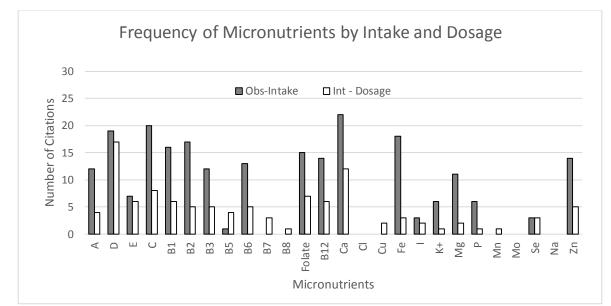


Figure 5A. Micronutrients cited by observation studies measuring intake and/or in intervention studies dosages

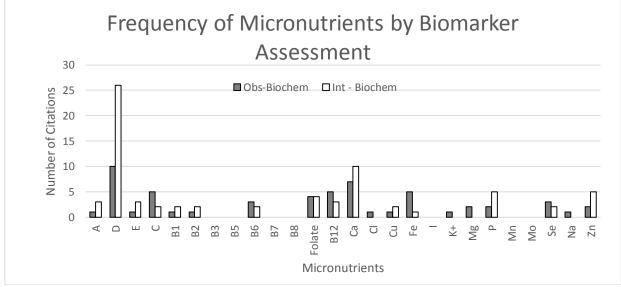


Figure 5B. Micronutrients cited by observation and intervention studies measuring biomarker status

#### Chapter 7

# Micronutrients on the Menu: Enhancing the quality of food in Long-Term Care for regular, non-therapeutic menus

# Abstract

Micronutrient (vitamin and mineral) deficiencies may exacerbate prevalent health conditions occurring in Long-Term Care (LTC) residents and current menus may potentiate this problem. A micronutrient-focused, food-first approach to menu planning may address this gap by emphasizing nutrient-dense foods. The objectives were to determine if: 1) selected LTC menus met micronutrient and Canada's Food Guide (CFG) recommendations, and 2) recommendations can be met through food alone with strategic menu planning. Regular, non-therapeutic menus (week 1, all meals) from diverse LTC homes (n=5) across Canada were analyzed for micronutrient content using Food Processor and CFG servings with EaTracker. Site dietitians confirmed menu analyses. Five super-menus were created and analyzed for comparison. Menus' nutrient content varied significantly across homes. Micronutrients of greatest concern were vitamins D (mean 8.90  $\pm$  5.29 µg/d) and E (mean 5.13  $\pm$  1.74 mg/d). Folate, magnesium, and potassium were also below recommendations. Super-menus of equal food volume met RDAs for all micronutrients but vitamin D (11.2  $\pm$  2.54 µg, mean 56% RDA), E (12.6  $\pm$  4.08, 84% RDA) and potassium ( $4018 \pm 489$  mg, 85%). Meeting most micronutrient recommendations is possible with creative and deliberate menu planning and knowledge translation of best practices is needed, as well as determining the potential cost of super-menus.

Key words: Long-term care; nursing home; menu planning; micronutrients; nutrition; aging

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# 7.1 Introduction

In 2011, an estimated 7% of Canadians (or 300, 000 Canadians) aged 65 and above were living in health care institutions, including Long-Term Care (LTC) Homes (1). This number is projected to double, where 750, 000 Canadians will be living in health care institutions by 2036 (1). The Canadian Malnutrition Task Force has raised the awareness of health care providers and the general population on the prevalence of malnutrition, and how it is impacted by many factors, including quality food provision (322,323). CMTF defines malnutrition as deficiency, excess or imbalance of energy, macronutrients and micronutrients that affects body tissues, impairs function and impacts overall health (322). Although Canadian estimates of malnutrition in LTC are elusive, it is estimated to occur in 20-60% of residents (5–9).

Adequate intake of a varied diet is needed to meet micronutrient requirements, although physiological factors including challenges with self-feeding, early satiation, taste changes, dysphagia, and decreased appetite are significant contributors to older adults' food intake, rendering them nutritionally vulnerable (13,14). Micronutrient (specifically, vitamin and mineral) status is critical to managing common health issues in LTC, including anemia, bone health (15), cognitive and functional status (16), immunity (17), infections, and wound healing (18). Micronutrient deficiency is a prevalent yet preventable form of malnutrition among older adults living in long-term care (LTC) (5,19–21). These deficiencies may further aggravate poor health and low intake, leading to a vicious cycle of malnutrition and decreased function, directly impacting residents' quality of life (22).

Menu planning in Canadian LTC homes is governed by provincial regulations (324), and typically planned considering *Canada's Food Guide to Healthy Eating* (CFG) to ensure variety (55). However, CFG may be inadequate in addressing micronutrient needs in menu planning, as

foods were not grouped into food groups based on nutrient content, but rather how food is traditionally consumed (i.e., legumes are grouped with meats because it is used as a substitute) (5,68). Consequently, micronutrient content of CFG choices differ greatly from choices within the same food group, and even the most nutrient dense food choices may still be inadequate to meet micronutrient recommendations. Dietary Reference Intakes (DRIs) provide micronutrient recommendations, yet planning based on this reference requires knowledge of intake distribution (69), which is currently lacking in LTC. Thus, menu planners use their professional judgment with the assumption that, by following CFG and serving a variety of foods, the DRIs will be met (5).

Compared to protein-energy malnutrition, relatively little research has been conducted on micronutrient malnutrition in Canadian LTC homes (26,259,325,326). In addition to the physiological changes with aging that affect food intake, it has been suggested that menus are not sufficient in micronutrients to meet residents' requirements (7). Analysis of menus from single Canadian LTC homes has shown discrepancies between CFG recommendations and DRIs (5,48), but did not always consider a comprehensive micronutrient profile for older adults (48). These findings require confirmation, analyzing menus from several homes and preferably across provinces to demonstrate the widespread prevalence of this potential problem. As meals provide the main source of micronutrients for residents (7) an analysis focused on meals will be sufficient to show discrepancies across provinces and as compared to guidelines. Given the prevalence of low food intake in Canadian (5,19,21,327) and LTC home residents worldwide (14,24,208,328), nutrient-dense menus with lower volumes of food are needed to help meet nutrient needs. It is also unclear at this point if the DRI can be met with the selection of more nutrient dense foods that are compatible with residents' preferences when planning menus.

# PURPOSE

This exploratory study aimed to assess the micronutrient content of several LTC menus to determine whether DRI micronutrient and CFG recommendations were met. A secondary aim was to determine if it was possible to meet micronutrient needs with lower volumes of food through development of micronutrient-dense menus.

# 7.2 Methods

## **Data collection**

Homes were recruited to provide their menus as part of a larger investigation on the acceptability of micronutrient fortification of common foods in LTC (329). Home dietitians/nutrition managers (n= 45) who had volunteered to be part of focus groups were asked to provide their home's menu for analysis. Homes that provided menus were either stand-alone or part of a small network of homes; none were part of a corporate chain. Ten menus were provided and five were chosen to represent provinces, type (for-profit/not profit (F/NFP)) and to promote diversity (i.e. culturally defined population). Further details on are not provided to ensure confidentiality of Homes where analysis was completed. One Home menu from British Columbia (NFP), Nova Scotia (NFP), Alberta (NFP) and two from Ontario (1F, 1NFP) were selected; the second home from Ontario included a unique cultural group. A maximum of five homes was chosen to ensure feasibility, but sufficient diversity to provide a more comprehensive analysis than conducted to date (5,48).

#### Menu analysis

Meals from the week 1 (7 days) non-therapeutic, regular texture menu were analyzed for each LTC. Beverage choices and break fast entrées were alternated each day to reflect residents' potential preferences. The first choice of all lunch and dinner entrées were selected for analysis. Serving sizes were obtained from each LTC. For mixed dishes (e.g. lasagna), recipes, descriptions, or brand names of purchased products were obtained. For single food entrées (e.g. chicken nuggets), a similar item from the nutrient analysis software was selected. Where recipes were not provided, generic recipes used from food distribution companies (e.g. Sodexo or Sysco) or from online recipe databases (e.g., allrecipes.com, canadianliving.com) were used. These recipes were adjusted, confirmed and verified by the site dietitian or nutrition managers to ensure they reflected the home's recipes.

Food and fluid items were entered into ESHA Food Processor SQL (version 10.12.0, ESHA Research, Salem, OR, 2012) to examine calories, protein, fibre and 21 micronutrients. As the first step, USDA choices were selected for entry as these provided the most complete micronutrient data. Where fortification influenced micronutrient values (e.g. grain and milk products) Canadian Nutrient File (CNF) choices were searched in the CNF database and relevant values were manually added to the ESHA program (152). To confirm food choices, eaTracker, a food database based solely on CNF values, was used for comparison and to calculate CFG servings in menu items and recipes (153). Menus' nutrient values were compared to genderspecific RDA/AIs for individuals aged 70 and above. Analyzed menus were provided to the homes for verification and adjustments made as required in portion size or selection of standard items in the food database.

## **Super-menus**

Super-menus (higher nutrient-density, lower volume; Table 13) based on commonly served foods were subsequently created to meet the RDAs for 11 micronutrients (thiamin, riboflavin, niacin, B6, folate, B12, C, D, calcium, magnesium, zinc) that are known to be poorly consumed by older adults in Canadian (5,15,19,21,26,48) and other LTC

(5,15,19,21,27,95,116,155,156,158,215). The analysis of the five diverse menus (above) provided the basis for developing the Super-menu. Specifically, herbs and spices were found to contain high levels of micronutrients and thus those consistent with recipes common to LTC were included. Some food items were also found to have different micronutrient contents depending on the variety [e.g. 1 cup red bell peppers (higher in vitamins A, C, and E) vs. green peppers; 1 cup white beans (higher calcium, potassium, and zinc) vs. black beans], and where appropriate, the most nutrient dense variety was selected for the Super-menu. Other strategies to increase nutrient density included use of yogurt or milk (higher vitamin D and calcium) to replace water, and cooking methods that maximized micronutrient content (e.g. steaming, reusing water that vegetables have been boiled in etc.). An iterative process was used to create these menus involving food/recipe definition, nutrient analysis, consideration of portion size, volume and calories, and subsequent refinement of recipes (recipes and the Super-menu are available from the authors). Consideration was given to having vegetarian options. Ingredients used to increase micronutrient content of recipes are shown (Table 14). Five daily menus were created to demonstrate the variety that could be achieved in menu planning.

#### Data analysis

Data were analyzed using SPSS (version 22, SPSS Inc., Chicago, IL, 2013). Descriptive statistics per home and across homes were summarized. Multivariate analysis of variance

(MANOVA) was used to detect significant differences among homes. Statistical significance was set at p<0.01 to account for the multiple tests performed. A two-tailed t-test was performed to analyze differences between Homes' menus (n=35) and Super-menus (n=5), with statistical significance set at p<0.05.

#### 7.3 Results

#### Current long-term care menus: Micronutrients and food group servings

Significant differences existed for nutrient levels determined from menus across the homes (Table 14). Between-home means were significantly different for calories, riboflavin, niacin, pantothenic acid, folate, calcium, magnesium, phosphorus, potassium selenium, and zinc (p<0.01). Home E had the highest caloric and protein contents, and the fewest micronutrients below RDA. However, caloric content did not always relate consistently to micronutrient content, as Home C met most RDAs despite having the lowest-calorie menu. Homes A and D had the second and third highest caloric content, respectively, but both had the same number of micronutrients below RDA. Home E micronutrient means were the most significantly different from all other Homes (p<0.01). Vitamin E levels fluctuated pending the inclusion of butter/fat at meals. When averaged over the entire week, none of the five homes met CFG recommendations for Grain Products; an average of 4-6 servings grain products were provided per day. Some homes were also below CFG recommendations for Vegetables and Fruits (1/5 below recommendation), Milk products (3/5 below recommendations), and Meat products (1/5 below recommendations) (data not shown). When analysis across home menus was averaged, vitamins D and E were below 50% of RDA/AI, and folate, magnesium (males only), and potassium were 50-75% below (Table 15).

#### **Super-menus**

Super-menus met recommendations for most micronutrients, and were closer to meeting recommendations for D, E, and potassium than current LTC menus (Table 15, Figure 6). Volumes and caloric content of foods served on Super-menus could not be reduced if the menu was to meet the RDAs, especially when attempting to meet vitamin D recommendations. Statistically significant differences between Home menus and Super-menus were seen with fibre, niacin, folate, vitamin E, calcium, iron, magnesium, phosphorus, potassium, sodium, and zinc.

# 7.4 Discussion

#### **Current long-term care menus**

This study provides a flavor of the micronutrient content of current Canadian LTC menus and a more comprehensive analysis than conducted to date (5,48). Previous studies have examined specific macronutrients (55) or multi-nutrient contents of Canadian LTC menus from single provinces (5,19,25,48,70), and emphasized the need and challenges of providing micronutrient-adequate menus. To our knowledge, this is the first study to examine micronutrient contents of menus from more than one province, and to attempt a food-first strategy to meet recommendations with a Super-menu.

Planning for Home menus was based on CFG recommendations and generally met these recommendations, yet average micronutrient contents varied among homes. Calcium intake was one of the few nutrients met in all homes and achieved by providing milk at every meal. Interestingly, the current menus demonstrate the potential of increasing nutrient density without increasing calories, as some homes with lower-calorie menus met more micronutrient needs than homes with higher-calorie menus. Yet, Vitamins D and E were consistently low in planned menus for all homes and the RDA was also not achieved in the Super menu. As vitamin D guidelines recommend supplementation of all residents to prevent falls (330), there is less concern about the inadequacy of this vitamin in the current planned menus or the Super menu.

These findings demonstrate that current planning guidelines alone are inadequate to address micronutrient needs, and more nutrient-dense strategies need to be explored in LTC (5,147) for key nutrients. Super-menus could not meet vitamin E and potassium requirements and other food-first strategies such as fortification may be required. The reality however, is that even with a menu meeting micronutrient requirements, intake is commonly poor in LTC (5,21,24,48). Menu planning is only one strategy to prevent malnutrition in this setting; mealtime eating assistance (203,331,332) or improving dining environments (333,334) are other potential strategies.

#### **Super-menus**

The exercise of developing super-menus presents several practice implications. Regular incorporation of herbs and spices to recipes not only enhances flavor, but can increase nutritional quality as they provide high levels of micronutrients in small quantities. It is also necessary to consider the micronutrient content of food variants, as subtle differences (e.g. black vs white beans) could mean substantial differences in nutrient density. Awareness of micronutrient content of ingredients may help menu planners choose higher micronutrient substitutes and create more nutrient-dense recipes. Education and training on the preparation and cooking methods that maximize micronutrient content may further help to improve LTC menus. This

analysis identified that almost all nutrient recommendations can be met with modest adjustments in menu planning.

Unfortunately, the devised super-menus were not lower in calories or food volume as compared to the original menus assessed. Reasons for not decreasing food volume with supermenus was the attempt to provide sufficient vitamin D (milk, eggs) potassium (vegetable and fruits); and vitamin E sources (nut butter, margarine), which led to increased calories.

Home menus are the main source of most micronutrients for LTC residents. The use of CFG with DRI recommendations, along with periodic examination of micronutrient components of food through nutrient analysis with CNF, will help homes to develop menus that meet most micronutrient recommendations. This process has demonstrated that it is feasible to improve the nutrient content of menus, but that investment in the process is required. Food funding continues to be an barrier to providing higher quality food in LTC for Canada (335). Moreover, Homes need to have nutrient analysis programs available and provide sufficient resources to complete the complex steps required to produce a menu with recipes that are acceptable to residents

# 7.5 Strengths and Limitations

A limitation of this study was that, no homes were from corporate groups and although requested they did not participate, potentially due to proprietary concerns. Corporate homes potentially have greater resources for nutrient analysis, which could lead to more nutrient dense menus. Additionally, only five menus were analyzed, representing four provinces. This is not a sufficient analysis to fully characterize Canadian LTC menus but is more comprehensive that studies to date (5,48,70). As compared to prior work, this study has several strengths including multiple menus used in analysis, across several provinces and the review of finalized recipes and

confirmation of analysis by the Homes' dietitians and/or nutrition managers. Furthermore, several steps were taken to ensure an accurate analysis such as comparison of ESHA results with eatTracker. Limitations for super-menus are that, while they were higher in micronutrients, these recipes have neither been trialed in LTC production kitchens, nor tasted by residents. Thus, feasibility in production and acceptability by residents have yet to be determined. Assessing cost of recipes is also necessary to demonstrate feasibility for use of super-menus within the constraints of raw food budgets for LTC. This analysis was not possible in this study as Homes and food distribution companies contacted did not provide the authors with a purchasing list.

#### **Relevance to Practice**

Menus are only one area to consider when trying to improve the nutritional status of older adults living in LTC. Based on this analysis, most micronutrient recommendations can be met with deliberate menu planning. Menu planning is complex and homes need to invest in training and development of nutrient dense menus. For those nutrients difficult to achieve through menu planning alone, supplementation (e.g. Vit D) or fortification (e.g Vit E, potassium) may be indicated.

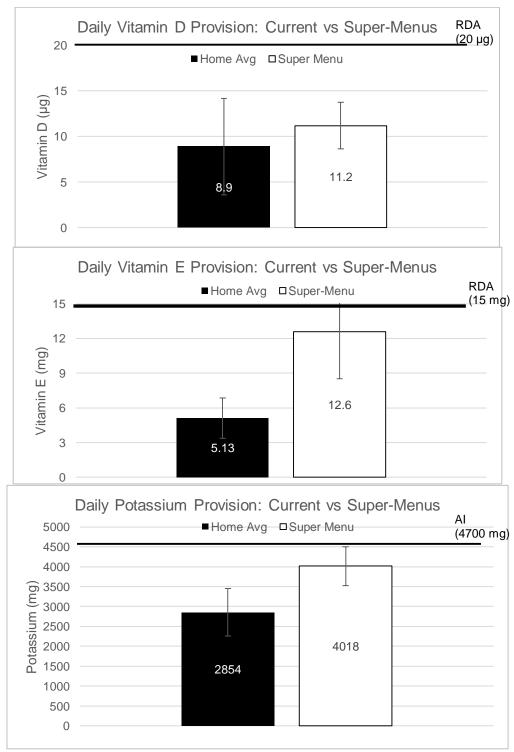


Figure 6. Comparison of LTC vs Super-Menus in meeting RDA/AIs for Vitamins D, E, and Potassium

#### Chapter 8

# Acceptability of Strategy: Webinar Focus Groups, Resident Focus Groups, and Key Informant Interviews

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#### Abstract

Purpose: Malnutrition is common in long-term care (LTC) residents, yet limited research exists on micronutrient deficiencies. Objective: This study used qualitative methods to explore the acceptability of a food-first micronutrient fortification strategy for LTC. Design & participants: Webinar focus groups are a novel method of conducting online focus groups, similar to a teleconference, to allow for the real-time, immediate response of traditional focus groups, without the physical presence and the need to travel, as was appropriate for this nation-wide study. Eleven staff webinar focus groups (n=45), expert key informant interviews (n=10), and five in-person family/resident focus groups (n=71) were conducted. Results: Stakeholders provided insight into benefits, concerns and potential solutions to minimize barriers and promote adherence to the strategy. Suggested solutions included development of outsourced/pre-made fortified products, mandatory training and clear protocols. Stakeholders can envision food fortification as a strategy to improve micronutrient status if products are easy to access and incorporate into current production systems. Yet, residents and families wish to be informed and have the potential to 'opt out'. Safety and efficacy also needs to be demonstrated before it is incorporated into standard practice. Conclusion: This work provides a strong foundation for developing a proof-of-concept micronutrient food fortification study for the prevention of deficiencies in LTC.

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#### 8.1 Introduction

Micronutrient (vitamin/mineral) deficiency is a prevalent yet preventable form of malnutrition among older adults living in long-term care (LTC) (5,20,21,199). Plate waste estimation suggests that approximately 1600 kilocalories is consumed (14), with even lower consumption by cognitively impaired residents (~1,100 to 1,200 kcal per day) (5). As menus are typically planned to meet 100% of residents' micronutrient needs, some residents may not meet their requirement due to low food intake (5). Little intervention research has been conducted on the prevention of micronutrient malnutrition in LTC (26).

Micronutrient deficiencies are often treated with strategies such as oral nutrition supplements (ONS) which attempt to ameliorate overall intake (5,336). However, waiting for signs of sufficiently low intake to stimulate this strategy means that subclinical deficiency is overlooked. Moreover, there are possible compensatory reductions in food intake at subsequent meals after ONS consumption, making the supplement a 'replacement' to regular food intake (260,337). Low adherence to ONS further reduces their long-term use (273–275). Micronutrient pills, although potentially preventative, are also used reactively (271). The risk of drug-nutrient interactions when administering vitamin/mineral pills (14), lack of coverage by drug benefit plans (338) and out-of-pocket costs for residents (119,278) are reasons for limited used in LTC. Research suggests that families (270,339) and providers (108,271) prefer a 'food-first' approach to address nutrition problems (5,21). Enriched/fortified foods have been proposed as such an approach (107,108). Most fortification practices focus on protein, which can be increased with naturally high foods (e.g. milk, eggs, or cheese) (107) or supplements (108) added to selected foods. While these strategies appear to improve energy and protein intake (109), these enhanced foods typically do not focus on improving micronutrient intake (107).

At present, there is no consensus on best methods for prevention of micronutrient malnutrition in LTC residents (26). In view of residents' average low food intake (5,27) and the recommended micronutrient levels to achieve nutritional adequacy (5,28), micronutrient fortification of key foods is a potential solution (29), yet has been rarely conducted and research to date does not identify best practices. This strategy is especially relevant for residents with insufficient nutrient intake but a stable body weight due to low levels of activity and energy requirement (19,26).

Assessment of the acceptability and feasibility of a *new* intervention should be done with end users prior to implementation, especially when the strategy requires changes in care processes (121). Determining the acceptability of micronutrient fortification with stakeholders who are closely aligned with planning, purchasing, preparing and serving food (dietitians, nutrition managers, cooks), will enhance understanding of barriers to implementation of this strategy. To date, there is minimal documentation on staff's perspective on food fortification in LTC. Further, few studies have examined residents' and family members' views of nutrition provision in LTC (270,339). Multiple perspectives of knowledge users will enhance our understanding of the acceptability of this strategy and will allow for triangulation of perspectives (136).

The purpose of this study was to determine the acceptability of a fortification strategy in LTC and to further develop the concept of this strategy based on diverse stakeholder input (e.g. instructions and protocols, the most appropriate foods for fortification, etc.). Specifically, knowledge users were asked to reflect on the potential of micronutrient food fortification, and identify their concerns and potential solutions when considering food production, delivery and consumption.

#### 8.2 Methods

Three stakeholder groups verified the acceptability of fortification of food in LTC: staff, expert key informants (KI), and LTC residents and families. Webinar focus groups were conducted with frontline nutrition staff, providing insight into both clinical and production issues with micronutrient fortification. Webinar focus groups allow for the real-time, immediate response of traditional focus groups, similar to teleconference systems, without the physical presence and the need to travel (160). Webinars have been previously used for training of staff (161) and students (162,163) and were thus considered a viable option for conduct of these focus groups. Online focus groups were conducted with webinar technology (WebEx<sup>TM</sup>, Santa Clara, CA)), a program that allows for teleconferencing at the same time as presentation on the internet (164). The webinar format traversed geographical barriers and allowed participants to join regardless of time zone or location. From the webinars, a number of participants who were knowledgeable on topics of interest (i.e. had conducted fortification) were identified and invited for individual in-depth KI interviews, along with additional KIs who were experts (e.g. government, food industry). Recognizing that webinar and KI informants were generally in favour of a fortification strategy, resident and families' views were ascertained via in-person focus groups. This study underwent ethical review and clearance by the Office of Research Ethics at the University of Waterloo (Ethics review #: 18558).

#### **Webinar Focus Groups**

Focus groups gather individual and interactive opinion and attitudes through a carefully planned framework of questions and discussions (159). The group format allows for interactions and discussions among participants and can contribute to further development of ideas and

concepts (159). On-line webinar technology offers the opportunity for on-screen presentations, group discussions, and immediate polling questions to engage all participants. Lower numbers of participants were recommended for online synchronous (real-time sharing) focus groups (165). Thus, several small focus groups (3-7 participants) were scheduled and conducted. The target participants were dietitians, nutrition managers and chefs working in LTC recruited through the Dietitians of Canada Gerontology Network and the Canadian Society of Nutrition Management (CSNM). Interested participants were sent an invitation e-mail containing: a detailed information letter outlining the purpose of the study and process, instructions to register, and a link to a presession online registration survey to collect pertinent demographics. Snowball sampling was also employed; participants of the initial webinars were ask to suggest potential further participants.

An advisory committee consisting of experts from the Universities of Waterloo and Guelph helped develop and review focus group discussion and polling questions. Open-ended questions with additional probes were used as a guideline to solicit information and discussion (167). Polling questions examined nutrients of concern for residents, current strategies used to address micronutrient needs, and participants' ratings on the appropriateness, feasibility and potential effectiveness of a micronutrient fortification strategy.

One-hour focus groups were conducted with WebEx<sup>™</sup>; initial sessions were conducted by the first two authors. Sessions were recorded to allow for transcription of the discussion. After the webinar, participants were emailed a link to a feedback form, which allowed them to provide further comments on the topic as well as to rate their experience with the webinar format and technology.

# **Key Informant Interviews**

KI interviews provided more in-depth information addressing questions with respect to the feasibility of the developing strategy that arose from the webinar focus groups. The advisory committee provided recommendations on various stakeholder groups whose insight and opinion on the potential strategy was desirable. Ten KIs were recruited by the primary author via email and those interested in participating were sent an information letter outlining the expectations for an interview and the study process. Individual KI interviews were conducted by the second author and the primary author took notes. A question outline was used to guide the interview. Sessions were conducted by telephone and digitally recorded for subsequent transcription. Verbal consent was obtained at the start of each session; interviews lasted approximately 45 minutes to 1 hour.

#### **In-person Resident/Family Focus Groups**

In-person focus groups were conducted at five LTC homes to obtain the opinions of family members and residents. Due to geographic constraints, only sites within an hour of the University of Waterloo were recruited. Initial contact was made by phone or email to nutrition management/dietitians to determine interest. Recruitment posters/letters were provided to notify potential participants of upcoming sessions. Group discussions were scheduled at the routine resident/family council/food committee meetings and a 20-30 minute time slot was allotted to the discussion. As a result, staff members were also present, although their opinions were not elicited; they acted as supports to the researchers for completing consent forms and helping with hearing impaired individuals.

Participants signed consent forms prior to the session and completed an anonymous feedback questionnaire on benefits and concerns about the strategy at the end of the session. This provided the opportunity to capture afterthoughts, as not all participants spoke during the discussion. These sessions were not audio recorded to keep the discussion informal and allay any concerns about confidentiality of the information, as well as challenges with soft-spoken participants on the digital recording. Extensive notes were taken by one of the two researchers present.

#### **Data Analysis and Interpretation**

Debriefing occurred after each focus group and KI interview between the first and second author to discuss overall impressions, key points, main areas of agreement or disagreement, and new data that resulted from each session (187). All webinar focus groups and KI interviews were transcribed verbatim prior to analysis, with identifiable information removed. Inductive content analysis was used to identify common points or concepts, patterns, and variations (185). This was the chosen analysis method, as this study aimed to explore the broad scope of the issue of fortification as a strategy. The first author and a student researcher each reviewed and coded half of the transcripts to complete an initial overview of the data using open coding (186). A code book was subsequently developed by the first two authors and the student researcher to assist with organization and categorization of the data (187,188). All transcripts were recoded after the development of the code book using selective coding. Exemplary quotes were identified. Memos were written throughout the analysis process to adjust and finalize the analysis.

Data from pre-session registration surveys, online polling questions, and post-session questionnaires were summarized and interpreted with descriptive quantitative analysis, and

where appropriate, supplemented with qualitative data. Other results not amenable to being counted were descriptively summarized with minimal interpretation (e.g. long-answer questions from feedback questionnaires) (159,187) and are presented as key concepts that address the purpose of the study; specifically i) concerns with micronutrient intake, ii) reflections on current strategies, iii) appropriateness of fortification, iv) promoting feasibility, v) determining effectiveness, and vi) overall acceptability of the strategy. Data from the three groups of diverse stakeholders is integrated under each key concept demonstrating triangulation and thus validity and credibility of results (187,188).

# 8.3 Results

Eleven webinar focus groups were conducted between March and April 2013, 10 KI interviews from July to August 2013, and five in-person resident/family focus groups between July 2013 and January 2014 (Table 16). All webinar and all but one key informant participant were female (Table 16), as there is a gender inequality in the LTC sector and nutrition-related professions (340). The majority of KI and webinar participants were dietitians. There was an even mix of gender and roles (i.e. family members, residents) for in-person family/resident focus groups. Shared key concepts are described below. Longer exemplar quotes are seen in Table 17.

# Concern about the intake of micronutrients in LTC residents

Polling results during webinars indicated that there was concern about nutrient intake in LTC residents, and specifically vitamin D, calcium, vitamin B<sub>12</sub>, and zinc (Figure 7). Webinar and KI participants associated certain micronutrients to specific food groups (e.g. vitamin D and calcium with dairy, thiamin with grains, magnesium with vegetables); low intake of these food

groups were suggested as reasons for concern. Dietitians noted micronutrients that were commonly prescribed for residents, in particular, vitamins  $B_{12}$  and D.

In addition to low intake, staff recognized inadequate provision by menus for certain micronutrients; Vitamin D was "a gap" (Registered Dietitian [RD]20) and "menus [were] not adequate" (RD22). A dietitian from a home that performed nutrient analysis found that the DRI for potassium was particularly difficult to meet, "due to the amount of food" and "the way [residents] eat" (RD33). Research findings were also reasons cited by dietitians for focusing on vitamin B<sub>12</sub> (RD17) and D (RD16). Physiological changes with age, low intake, and low biochemical values were among the reasons noted by participants for why micronutrient fortification might be appropriate for LTC residents

Conversely, certain micronutrients were identified to be problematic for a home-wide fortification strategy due to contraindications for health conditions or fear of toxicity. This included potassium and phosphorus for renal conditions (Nutrition Manager [NM]5), long-term zinc supplementation affecting absorption of other nutrients (RD20), and potential toxic accumulation of fat-soluble vitamins (RD6). Of particular interest was calcium, where staff hesitated to supplement due to recent changes to remove calcium supplements from residents' medication lists (Family Council [FC]3 staff) as a result of potential increased cardiovascular risk. Accordingly, staff was wary of supplementing calcium outside of food sources and preferred to treat calcium on an "individual basis, depending on dietary intake" (RD20).

#### **Reflections on current strategies**

Current practices were mentioned as a barrier to provision of adequate micronutrients from food for older adults. For instance, menu planning currently focuses on macronutrients,

with the assumption that micronutrients would be met in the process (RD16, RD17 – Table 2.A1, A2). Moreover, certain homes may not be equipped to do micronutrient analysis of menus and homes with pre-analyzed menus "don't know how accurate it is" (RD17). Miscommunication between guidelines and practice may also be a barrier. For instance, LTC homes may plan menus to the Food Guide, focusing on quantity of food to meet food guide servings (Key Informant [KI]4 – Corporate LTC Menu Planner – Table 2.B), when the original intent of this guidance from the government was to provide a variety of food (KI7 – Ministry of Health personnel – Table 17). This demonstrates a need for good knowledge translation when implementing strategies into practice.

Pills were the most common strategy described to address potential micronutrient deficiencies, yet this was unsatisfactory to many participants. Provision of nutrients in pill-form "appears medicinal in nature" (RD28) rather than food. Additionally, the shift to "reduce polypharmacy" (RD26, NM36) in LTC meant physicians were "quite reluctant to supplement with a multivitamin" (RD15). Potential costs incurred to residents for pills not covered by drug benefit programs and the difficulty in finding a single supplement providing complete micronutrients for older adult were also mentioned. Staff noted that use of oral nutritional supplements (ONS) could reduce intake at subsequent meals and may not provide other nutrients that food does (NM36). The process of ONS administration was also noted as redundant and reactive (KI2, Health and Marketing Specialist for Food Supplier).

Interestingly, some participants preferred provision of ONS as a combined "top up" (RD22) approach that provided calories, protein, and fluids *plus* micronutrients. One family member preferred administration of vitamins for its accuracy and simplicity for tracking (Family/Resident Council [FRC]2). Overall, LTC homes have strategies to address nutrient

needs and low food intake, yet these may not be micronutrient-specific, are more medical than food in nature, and compliance remains an issue, leaving room for alternative food-first micronutrient strategies in LTC.

# Appropriateness of a fortification strategy

When considering if fortification of common foods was appropriate in the current LTC system, cost was "one of the biggest barriers..." (KI1, Industry Brand Manager). The given food budget and cost of food meant that any new strategy had to be cost-effective for acceptance within the industry. Precision is needed for micronutrient dosages. Participants were also concerned with staff's ability and accuracy in adding fortificant to selected foods in-house (KI5 – Culinary expert), noting current compliance issues with supplemental protein and thickeners due to misinterpreted instructions and lack of time (NM36). To be appropriate, the fortification strategy would need to be easy to implement with an accurate, foolproof procedure for staff to follow (RD17).

Further concerns for appropriateness included the classification of fortified products as food or as medications, which had implications on the personnel providing the product. Since most dietary staff and health care aides providing assistance at meals have minimal training, the potential for errors with in-house fortification of food products was a noted limitation (RD9). Hence, some webinar and KI participants identified that an outsourced product would be the best approach to promote consistency and safety. Staff was concerned with "too much… fat-soluble [vitamins]" (RD6). Family members were also concerned with the risk of toxicity for residents with good appetites who may consume extra portions (FC4). Thus dosage and procedures for daily use would need to be clearly defined and monitored.

For residents, taste was a top priority. Residents noted taste changes with age and were concerned fortification could change tastes of favourite foods (Resident Council [RC]1). Family members were also concerned that taste alterations with fortification may further limit intake for persons with dementia who were picky eaters (FRC2). Family/resident councils thought fortification was a good strategy but if implementation meant that other activities (e.g. staff providing eating assistance) would be jeopardized, than they stated that, "fortifying foods would go on the back burner" (FRC5). Other family members noted that fortification would not be enough to meet the needs of some highly vulnerable residents who consume very low volumes of food (Family/Resident Council (FRC) 2). The desire for choice was voiced by residents and family who wanted the decision to voluntarily opt out of consuming fortified foods (RC1). Findings suggest that a flexible approach to fortification, with variety in food products and ensuring that sensory qualities are maintained are necessary for stakeholders to consider the strategy as appropriate for LTC.

Overall, the participants appeared to find the strategy acceptable. Over half provided a rating of 4 (n=17 of 40; 43%) or 5 (n=6), the maximum score, for the appropriateness of in-house fortification as a strategy to improve micronutrient intake. Appropriateness of outsourced fortified food was similar where the majority of participants provided a rating of 4 (n=13 of 31; 42%) or 5 (n=6) (Note: totals are different as appropriateness of outsourced fortification was added after webinar session 3). Understandably, all participant groups requested additional evidence of effectiveness of the fortification strategy, including improvements in serum markers of nutrients, and assurance of no taste changes so as to be convinced of the appropriateness of a fortification strategy.

# Promoting feasibility of a fortification strategy

Several webinar participants had trialed fortification in LTC. These food-first approaches included the addition of flax (RD26), skim milk (RD30), chickpea flour (KI2), chocolate milk (RD15), or Carnation Instant Breakfast® (RD15). However, such strategies focused on dietary fibre, protein and energy, and although enhancement of other foods with these ingredients may overlap to provide micronutrients (e.g. vitamin D and calcium with milk), the majority of these were not micronutrient-focused efforts. One KI reported on a long-term micronutrient food fortification program (calcium in a whipped topping) in several homes in Nova Scotia, where the purpose of the fortification strategy was "to get away from the medication cart...[and to] put it in our food" (KI3, dietitian). This strategy required buy-in and collaboration with stakeholders at multiple levels: experts (endocrinologists, geriatricians, physicians, pharmacists), home administrators, knowledge users (dietitian, cook, baker, dietary manager) and end-users (family/residents). Taste-testing began at a staff level, then to family councils, and approval at the Ministry of Health level, with funding obtained for the strategy. This example provided evidence that a food-first approach to micronutrient fortification for the general LTC population was not only appropriate, but also feasible. It also provided a framework for exploring this concept with other participants.

Identifying food carriers (vehicles) for fortification based on common foods most residents enjoy and can consume was required to make the strategy feasible. Participants offered various recommendations for food vehicles (Table 18). Breakfast was the "best meal of the day," and several staff suggested food vehicles in this category (RD16, RD20, RD35). Fluids, including broth, coffee, juice, and milk were recommended. Soup was frequently mentioned as "a comfort food [that] ... is consumed... [even by] people with no appetite" (RD15). Dessert was

the most common suggestion among participants. Ice-cream was suggested as "number one on [residents' preference] list," and is preferred across various cultural groups and diets (KI4). Condiments and toppings were also suggested for their small, pre-measured packages and versatility for use with different foods. Participants suggested the aforementioned foods vehicles over entrees (e.g. meats or vegetables) for ease of incorporation (KI4). Overall, staff preferred foods addressing different texture needs (e.g. puddings, oatmeal, mashed potatoes). "Variation" (KI5) of food vehicles or a "multipurpose item" (KI2) are also needed" "to prevent resident boredom" (KI3) and "maximize the opportunity to consume" [foods] (KI7).

Strategies for in-house fortification included provision of clear protocols and incorporating fortification into part of the recipe (RD28). A systematic framework of the food fortification process, from assessment to monitoring, along with clear direction and assignment of roles (KI7). Involvement of staff and stakeholders at multiple levels to increase resident and family's awareness of the need for micronutrients and to help them make informed decisions was noted across participant groups as a means to increase adherence (NM5). Due to these feasibility concerns with in-house production, outsourcing a food that was fortified was seen as a preferred option to minimize time required to prepare the product, and to ensure consistency.

# Determining the potential effectiveness of a fortification strategy

Staff webinar participants rated the overall potential effectiveness of the micronutrient fortification strategy in meeting residents' needs on a 5-point Likert scale (5=very much). Participants agreed that the concept of the strategy could be effective (rating of 4 (n=17 of 39 responses) or were neutral about the strategy (rating of 3 (n=11)). [Note: if two or more participants were on the same phone line/computer station for the call, only one response was

possible]. However, participants expressed the difficulty in determining the effectiveness of the strategy without full knowledge of the content and format of the final product (NM36).

Cost was a barrier that could affect the appropriateness of the strategy for LTC and participants suggested that it was necessary to show that benefits outweighed the cost (KI1). Family members also requested evidence of effectiveness of the strategy through research, and testing of residents' serum micronutrient levels to demonstrate need and improvements with this strategy. Likewise, they mentioned that funding could be "prohibitive [for the strategy] due to budget constraints" (FRC2). Although preference of pills over food was uncommon, it suggests the need to address and overcome administration, tracking and monitoring issues with micronutrient food fortification.

Residents valued that the strategy may "improve [residents'] quality of life" (RC3), yet additional factors, including ethical issues with palliative residents, still need to be addressed before effectiveness could be fully determined (FC4). At this point, participants viewed food fortification as a potentially effective concept to address micronutrient malnutrition in LTC, but more development and proof-of-concept research is required before effectiveness can be accurately assessed.

# **Overall acceptance of a fortification strategy**

Participants generally supported the concept of micronutrient food fortification as a potentially effective, food-first strategy to address micronutrient deficiencies, stating that "trying to use real foods [is their] preference to a supplement" (NM36). Feedback questionnaires from 24 residents and family members rated the overall acceptability of the strategy on a 5-point

Likert scale (5 = very much); the majority rated the strategy as 4 (n=10) or 5(n=8). Family members welcomed a strategy that enhanced the nutrient profile of LTC meals (FRC2).

Staff stated that "to add [micronutrients] to foods that residents *enjoy* eating" would be a "better accepted" strategy (RD26) than current strategies. At the very least, participants thought this provided "a good alternative (FC4)" to current LTC strategies used to address micronutrient deficiencies. Participants also saw the benefits of increasing residents' food and nutrient intake, even in small amounts (NM3, NM36). In sum, the strongest benefit of micronutrient food fortification was its long-term, cumulative effect rather than immediate impact:

I can't predict they're going to get 100% of it. But I can... predict if I give it consistently daily, it adds to their nutrient intake. So it works! ...We've had falls, and...a significant reduction in broken bones! So something's workin'. (KI3, RD with food fortification experience)

Much work needs to be done to solidify this fortification strategy, yet findings from this study confirm that a food-first strategy addressing micronutrient needs is a "move in the right direction" (Chef7).

# 8.4 Discussion

Fortification has been noted as a potential cost-effective, long-term strategy to address micronutrient deficiencies in vulnerable groups with known low intake (341). Ongoing concerns about population-wide food fortification has been documented, ranging from differences in individual absorptive ability and needs (342), to public health issues of appropriateness and availability of fortified foods (343), to changes in food properties due to reactions with more effective but reactive forms of these micronutrients (344). Food fortification using micronutrients

specific to LTC residents' needs is a novel approach, where the objective is to provide a lowlevel dosage to prevent or delay long-term complications (similar to a multivitamin), rather than provide short-term or immediate reversal of a micronutrient deficiency. This study aimed to determine acceptance of a potential food fortification strategy from the perspectives of various stakeholders, and to gather feedback to inform this strategy. Due to the novelty of this approach, little prior research is available for comparison and required participants to assess the concept in an abstract stage of its development.

Previous work has examined pre-made (112,115) and home-produced fortified products (119) in LTC. These studies considered some issues such as sensory changes (119), appropriateness of texture (119) and food habits and preferences of residents (116), areas of consideration consistent with this research. Potential food vehicles mentioned by our participants were also similar to those used in previous studies, which included condiments (e.g. butter) (116), beverages (e.g. juice, milk) (117,301), snacks (e.g. cheese) (115), sides (e.g. bun) (112) and entrées (119). Yet the complexity of food fortification identified in this study, especially the process and procedural considerations required, have not been discussed in prior research. Efficacy of selected micronutrient fortification has been demonstrated (112,115– 117,119,301) and examined using vitamin-only preparations (119) or targeted to specific health conditions (112), but effectiveness of a population-wide fortification strategy using many micronutrients is still required. Given the known low food intake in LTC (19,21), and potential inadequate micronutrient contents of LTC menus (5), this strategy is logical. However, the LTC setting may require a separate assessment when considering these issues. This study has provided a foundation for development of such a strategy. Specifically, the desire for residents to be

informed of the micronutrients chosen in the fortification formula was voiced by all participant groups, demonstrating the value in acceptability testing with knowledge and end-users.

This study used multiple methods to gather input from diverse participants and is the first published report focused on acceptability testing of a food-related intervention for LTC; yet it had some challenges and limitations. Online focus groups in the literature are largely done as chat-forums (160) and lack the immediate feedback component that in-person focus groups provide (161). Webinar focus groups are an innovative technique for research, allowing for realtime conference and voice discussions, while facilitating ease of participation for those in geographically separate locations. One suggestion for future studies using webinar focus groups is to limit group size to 3-5 participants to promote participation in the discussion and reduce crosstalk. Focus groups with similar participant composition (e.g. all dietitians) may minimize power imbalance and allow participants to speak more openly (159). Voice-only webinars may be beneficial as webinars may be seen as less threatening than face-to-face, providing a sense of detachment/remoteness that allows participant to freely divulge information (165,345). Participants provided feedback on the webinar technology, process and content through an anonymous feedback questionnaire. Participants' main concerns were regarding voice delay/overlaps. Suggestions for improvement included: using phones over computers (better clarity), including type-in chatting (to capture all comments), having test/practice sessions, and additional cueing/direction from facilitators. The high level of response for these questionnaires (84%, n = 38/45 - data not shown) suggested a high level of engagement in the webinars. Focus groups with LTC residents had some challenges, as many residents had functional and cognitive deficits, and at least one staff member was present to help facilitate the consent process and to help residents communicate. The inclusion of staff in the room may have affected participants'

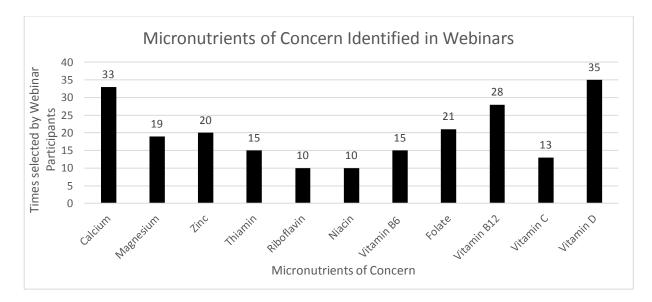
responses as they may have felt less comfortable reporting issues or concerns. The inclusion of an anonymous feedback questionnaire offered an extra venue for residents and family to share their thoughts in a more private manner.

The LTC setting is unique in that the same food is offered to all residents. Thus, it is essential that the selected food vehicle be well-liked and consumed by all residents for this strategy to work. Provision of micronutrient-fortified food options at each meal may increase the likelihood of residents accepting the fortified foods, and the choice of in-house and outsourced food vehicles to adjust to different LTC's production systems may facilitate the uptake of this strategy. Yet an opt-out may still be needed for residents' potential allergies/intolerances to the chosen food vehicle, or simply because residents or family wish to do so. More effort is needed to help residents and family members understand the potential benefits of the strategy through established efficacy and potential health improvements with the use of micronutrient fortification. Given the low food consumption in LTC (5,21), it is likely that most will benefit from a low-level dosage of micronutrients to meet dietary recommendations. Future work should continue to develop protocols for implementing the strategy, such as whether or not triggers are needed to direct micronutrient food fortification to target poor eaters in LTC (e.g. if resident eats <50% of meals consistently, s/he should receive the food vehicle), or whether the current LTC population-wide approach is still appropriate. A current knowledge gap is an understanding of food intake over more than one day in a large random sample of residents from diverse LTC homes to fully understand the potential variation in micronutrient intake. Outsourced products were preferred as they overcome feasibility issues associated with consistency in preparation and thus safety, yet any product has to be cost-effective as food budgets are limited in LTC. Finally,

once the strategy is developed, creation of effective protocols to train staff, along with tracking and monitoring residents' intake of the food vehicle are needed.

# 8.5 Conclusion

This study provides a comprehensive examination of diverse perspectives on the possibility of micronutrient food fortification for LTC. Micronutrient food fortification appears to be acceptable if some considerations are addressed, including development of protocols, proper education and informing of staff, residents, and family, and exploring alternative implementation solutions (e.g. outsourcing the product). Proof-of-concept work is needed as well food sensory evaluations to ensure that taste, texture, smell and colour of food vehicles are not influenced. Trialing the fortification in actual LTC production systems, and a clinical trial to provide evidence of benefits of the fortification strategy are also crucial. It is uncertain if this strategy will surpass, equal, or fall short of current strategies, but participants confirm that it is a needed area of future research and could be an acceptable strategy. As stated by a resident when asked about the acceptability of this strategy: "Nothing ventured, nothing gained."



**Figure 7**. Frequency of micronutrients identified in webinars as being of potential concern for LTC residents. N=45.

#### Chapter 9

# **Discussion and Conclusion**

# 9.1 Prior Research

Studies have shown that many factors affect Long-Term Care (LTC) residents' micronutrient (vitamin and mineral) intake, including challenges with self-feeding, early satiation, taste changes, dysphagia requiring modified diet textures (27,50), poor dental status (49), and decreased appetite, rendering them nutritionally vulnerable (13,14,198). Thus, micronutrient deficiency is purported to be prevalent among older adults living in LTC, yet this literature is disparate and limited in some areas, especially with respect to interventions (5,21,199).

Accordingly, this thesis explored the gap in the understanding of micronutrient malnutrition in LTC, and extended strategies used to improve micronutrient intake. This thesis' overall objective was to investigate the potential and extent of micronutrient malnutrition in LTC and identification and development of food-first strategies to improve micronutrient intake. The four specific research questions that guided this research were:

(1) What is the range of micronutrient intake and status (biomarkers) in LTC from the literature, and how these ranges compared to standard references to determine the potential for micronutrient malnutrition?

(2) What feasible and effective non-oral nutritional supplement interventions for improving micronutrient status were effective in LTC residents?

(3) What is the adequacy of micronutrient provision in LTC menus when compared to the DRI? Can a food-first menu planning strategy provide sufficient nutrients to meet residents' requirements?

(4) Is a food fortification strategy considered acceptable by various stakeholder groups?What provisions are necessary to enhance acceptability?

In this chapter, key findings are explained, compared, and contrasted with prior literature. The significance of the findings, strengths, and limitations of this thesis are also discussed. Lastly, implications for future research are made.

# 9.2 Positioning of Key Findings within Existing Research and Implications of Research Findings

At the start of this thesis, the candidate recognized that low intake of micronutrients may be of concern in LTC, given the prevalence of low food intake (5,21), inadequate micronutrient provision in LTC menus (48,70), as well as frequency of micronutrient supplementation in practice (58,103). However, careful summarization and examination of the literature on residents' micronutrient status based on biomarkers suggests that exposure may be adequate. Efficacy of supplementation and micronutrient fortification were also examined in this thesis. While both were able to improve micronutrient intake and certain biomarker statues, it was not possible to determine whether one strategy was more effective than the other, as different micronutrient formulations and dosages were trialed. Moreover, simple food-first strategies such as careful menu planning were able to improve and meet recommendations for most micronutrients. Thus, the need for micronutrient food fortification in LTC may not be as urgent as initially thought, and may be more appropriate as a back-up strategy after food-first interventions have been trialed. The steps taken to inform these decisions are discussed below. Triangulation is a research technique that combines different but complementary sources of data to answer a particular research question (195). By comparing results from different methods and data sources, intrinsic weaknesses or biases of an individual method can validate and/or expand on the other, improving not only the understanding of the research question, but also the overall credibility and validity of the study (195).

Five types of triangulation were identified by Guion et al. (2011): 1) data triangulation, 2) investigator triangulation, 3) theory triangulation, 4) methodological triangulation, and 5) environmental triangulation. The first 4 types of triangulation were used in this thesis. Their contributions to the findings and overall conclusion are discussed.

*Scoping Review-Observational studies (SRO):* The scoping review methodology allowed for mapping and categorization of a disparate literature related to micronutrient food fortification in the LTC setting. The first scoping review (observational studies) examined micronutrient intake and status data of LTC residents. Intake studies (e.g. diet histories, food frequency questionnaires, estimated food records, weighed food records) and studies with biomarker status were collected. Data was quantitatively analyzed by categories and frequencies of appearance. From intake studies, this review identified **vitamin D, folate, calcium, vitamin E and B6** intake to be consistently <50% RDA in LTC residents examined. For biomarkers, more than one study found biomarkers to be below AMA and/or CDC cut-offs for **vitamin D, C, folate, and iron**. It is interesting to note that vitamin D and folate were identified by both intake and status studies, but that the more objective biomarker shave been recognized as a more objective method of assessing dietary consumption and exposure (346). Yet, not all nutrients examined in dietary status studies were examined with biochemical markers. Specifically biomarker status of vitamin

B3, pantothenic acid, biotin, iodine, and manganese were not assessed in any of the identified citations, and thus it is not known if poor intake transfers to abnormal biochemical status. Micronutrients where only one citation with biomarkers was found included: vitamins A, D, E, thiamin, riboflavin; and chloride, copper, potassium and sodium. Magnesium, phosphorus, and zinc statuses were only assessed by two studies. Hence, of the key issues with biochemical analysis work to date is the dearth of literature reporting biomarker statuses of nutrients.

Issues with recall bias and estimation errors are weaknesses associated with dietary intake assessment methods that may make it a less reliable method (31,346). While varying lengths of dietary assessments were conducted (1 to 21 days), the majority of studies were 3-day weighed food records (n=5 of 16 WFR, 31%) and 3-day estimated food records (EFR) (n=8 of 11 EFR, 73%). Research has identified that micronutrients require differing lengths (e.g. days) of assessment to account for dietary variations of consumption to provide an accurate estimate of intake (231). Interestingly, the suggested number of days to account for dietary variation for micronutrients all exceed 3 days, with calcium requiring 10, iron 12, and vitamin C requiring 36 days (231). Thus, the accuracy of 3-days of intake for correctly identifying potentially inadequate intake is questioned. Yet the purpose of an SR is the aggregation of data across studies and the consistency identified for some nutrients suggests a true deficit in intake as data cross methods, regions and at risk characteristics or residents.

The use of dietary biomarkers also helps address this concern, as biomarkers are objective methods of micronutrient status in the body (346,347), and can reflect micronutrient intake (39,346,347). Of course, biomarkers may reflect both intake and body store levels of micronutrients, making it difficult to untangle the effects of dietary intake alone (39,347). For instance, while serum retinol is a reliable measure of vitamin A status, levels do not change until

levels of deficiency are reached, and this biomarker is not sensitive to smaller changes (39). In this review, the one study examining vitamin A status measured serum carotene, which is affected by non-nutritional factors as well and is thus not specific to intake status (39). This highlights a key challenge with using biomarkers of nutrients to assess adequacy of intakeseveral biomarkers are not sensitive and/or specific. Circulating 25-hydroxyvitamin D (25(OH)D) is a common measure of vitamin D status, but reflects both dietary intake and skin synthesis, thus is not specific to intake alone. However, given the nature of LTC residents and low frequency of sun exposure, this biomarker may be more appropriate for LTC. The other vitamin D biomarker identified from the studies was 1,25(OH)<sub>2</sub>D, which is a functional biomarker and not a status marker. Moreover, it is tightly regulated and levels change based on kidney function, making it a less useful biomarker for the elderly (39). Thus, even when micronutrient biomarkers are documented, their appropriateness and accuracy in assessing status is not guaranteed. However, triangulation of dietary and biomarker data can help identify which micronutrients are potentially insufficiently consumed by residents in LTC, and have specifically identified these to be vitamin D and folate.

*Scoping Review-Intervention studies (SRI):* The second scoping review summarized and examined the extant literature to determine non-oral nutritional supplement interventions that are feasible and effective for improving micronutrient status in LTC residents. In particular, this review found pill-form micronutrient intervention studies to be more common than fortification intervention studies, with **vitamin D and calcium** as the most common micronutrients to be included in both forms of intervention. This was not surprising as these nutrients were identified to be low in intake (vitamin D, calcium) and biochemical status (vitamin D) by observational studies, and there is a considerable concern about the functional effects of deficiency, in the form

of falls and fractures in residents living in LTC (106,348,349). The repetition of micronutrients of concern from observational studies that were found in intervention studies confirm that these are, in fact, micronutrients that residents may be at risk of deficiency for, and supplementation or fortification interventions may be effective at improving status or decreasing risk of these micronutrient deficiencies. However, whether fortification or supplementation had higher efficacy could not be determined, as adherence and compliance likely affects efficacy, yet not all studies reported on this, and no study compared fortification to supplementation.

Pill form studies examined physiological (i.e., <RDA) (99) and pharmacological levels (i.e., > RDA) of nutrients (94,205,287,297), while fortification typically only studied physiological levels (115,117,301). As well, the purpose of fortification was focused on prevention (117,301), whereas pill studies were sometimes used to correct known or perceived deficiency (94,205,295). Lower doses in fortification studies may have been due acceptance and potential taste changes with nutrient levels above the RDA; no fortification study examined minerals because of this concern. Yet, long-term acceptance and adherence with lower dose fortified foods may be greater than pill forms. Until such studies are conducted comparing these forms of intervention, especially for multi-nutrient formulations to combat general low intake, conclusions about which is more efficacious for prevention of micronutrient deficiencies is unknown. Certainly, treatment of deficiency is more efficacious with pill forms that can deliver pharmacological doses.

*Menu Analysis (MA) and Super-Menus (SM):* As informed by the scoping reviews, vitamin D and folate were micronutrients of concern for both intake and biomarker status, while several other micronutrients were low in intake or biomarker status. Interventions also focused on vitamin D, so it was anticipated that menu analysis would demonstrate provision at levels for

this nutrient to be below the RDA. Menus were quantitatively analyzed, and micronutrient contents were compared to DRI ranges. As anticipated, menu analyses identified vitamin D and folate levels in menus to be below RDAs for older adults. However, vitamins D (mean  $8.90 \pm$ 5.29  $\mu$ g/d) and E (mean 5.13  $\pm$  1.74 mg/d) were the nutrients consistently lowest across homes, and supports the SRO findings that vitamin E may also be a potential problem. From SRI findings, only one citation on vitamin E biomarkers was identified (54), and no AMA or CDC cut-offs are available to assess biomarker status. Thus, lack of data may lead to a perception that a micronutrient is not of concern for deficiency when, in fact, the absence of data can lead to this erroneous conclusion (see Figures 6A and 6B). Nonetheless, magnesium, and potassium (also identified in SRO) were also below recommendations. These findings verify the need to address these micronutrients of concern, yet presents another level or area for which to target efforts for micronutrient enhancement – the menu planning stage. Although low intake is a real issue in LTC (5,21), this menu analysis revealed that inadequacies in nutrient provision may be an issue as well. These findings echo those of previous researchers' with LTC menu analyses who have documented that LTC menus are not meeting all micronutrient requirements, and have identified challenges in planning menus that meet recommendations (5,25,48,70).

Thus, to determine whether or not it was possible to develop a food-first, menu planning strategy that meets micronutrient requirements in LTC, five micronutrient-dense super-menus were created and analyzed with a nutrient analysis computer program (ESHA Food Processor). Because of the consistency in findings from the scoping reviews and menu analysis that vitamins D, E and potassium were low, it was anticipated that these nutrients would be the hardest to meet. Other nutrients identified in the SRO to be low were not always consistent with the menu analysis, and it was assumed that these could be met through careful menu planning.

Super-menus of equal food volume and caloric level met RDAs for all micronutrients but vitamin D ( $11.2 \pm 2.54 \mu g$ ), E ( $12.6 \pm 4.08 mg$ ) and potassium ( $4018 \pm 489 mg$ ). In summary, while super-menus met recommendations for all but three micronutrients, and were closer to meeting the DRIs for these than were regular Home menus, findings suggest it is not possible to meet all micronutrient requirements with food alone without increasing volume of food provided. Consequently, this leaves room for micronutrient-enhancing strategies beyond natural food alone, especially to prevent deficiencies in those with low food intake.

Acceptability Testing (AT): The last substudy of the thesis was analyzed quantitatively and qualitatively. Findings from previous sections have indicated that: micronutrient intake may be inadequate in LTC and may affect micronutrient status, micronutrient supplementation and fortification may be effective at improving micronutrient intake and status, and menus' micronutrient levels could be enhanced by more purposeful planning with higher quality and micronutrient-dense ingredients. Yet, menu analyses and super-menu findings suggest that not all micronutrient needs could be met with food alone without an increase in volume. Given the prevalence of low intake in LTC (19,350,351), other strategies to improve micronutrient intake are needed. The scoping review on intervention studies identified supplementation and fortification to be feasible methods to improve micronutrient intake. As polypharmacy continues to be an issue in LTC (58,102,103), and families and staff have been found to prefer food-first strategies to improve nutrition for residents (352), it was decided that a micronutrient food fortification formula should be researched for LTC. Prior to implementation of an intervention study, stakeholders' input should be gathered as this has been shown to positively impact longterm adherence of strategies (121).

Acceptability testing in this thesis included staff webinar focus groups, expert key informant interviews in-person family/resident focus groups. Stakeholders provided insight into benefits, concerns and potential solutions to minimize barriers and promote adherence to the strategy. The most common micronutrient of concern was vitamin D, yet some were concerned with excessive micronutrient intake as well. For instance, with recent findings of the relationship between calcium supplementation and increased risk of cardiovascular disease (106,292), and reductions in calcium supplementation prescriptions in LTC, staff and family members were concerned about adding this micronutrient to formulations. Thus, micronutrients of concern for stakeholders may be affected by trends of the times (e.g. folic acid fortification, recent interest in vitamin D with the updated DRI recommendations). It was also noted in the SR that micronutrients studied in individual citations were likely affected by research interest, which did not necessarily coincide with the potential true prevalence of deficiency. Comparisons of citations on micronutrient intake to DRIs and comparisons of micronutrient biomarkers to AMA and CDC cut-offs indicate that these micronutrients, in fact, did not meet micronutrient recommendations or adequacy cut-offs, and that their importance is greater than the frequency of citations and trends would suggest. In the triangulation of methods, SR results were shared with stakeholders to overcome potential misconceptions about micronutrient status and the potential for fortification to meet needs.

Overall, stakeholders were receptive of micronutrient food fortification, yet wanted more demonstration of efficacy of this strategy to prevent micronutrient deficiency in LTC. Examples of fortification vehicles and methods from prior research identified in the SR were shared with stakeholders to help to develop a strategy that they believed could work in the Canadian LTC context. Suggested components of the strategy included development of outsourced/pre-made

fortified products, mandatory training and clear protocols. Stakeholders can envision food fortification as a strategy to improve micronutrient status if products are easy to access and incorporate into current production systems. Residents and families wish to be informed and have the potential to 'opt out' of home-wide formulation. Safety also needs to be demonstrated before it is incorporated into standard practice. This work provides a strong foundation for developing a proof-of-concept micronutrient food fortification study for the prevention of deficiencies in LTC.

#### **Findings from Hypotheses**

The first hypothesis that micronutrient malnutrition exists in LTC (as evidenced by assessing micronutrient intake and biomarker statuses), where it was expected that both micronutrient intake and biomarker statuses will be low in the LTC group, was partially supported. Intake was indeed identified to be low in LTC using several dietary intake methods. However, much fewer biomarkers were identified to be low and/or deficient. A reason for this – as previously mentioned – may be owing to the dearth of useful biomarkers for measuring micronutrient status, as well as having fewer studies measuring biomarker status compared to studies measuring intake (See figures 6A, 6B). This serves as a call for future work on the identification and testing of biomarkers specific to micronutrient status.

Second hypothesis: From the scoping review intervention studies, the hypothesis of micronutrient food fortification being able to increase biomarker levels of LTC residents was supported for vitamin D, but results are inconclusive for calcium, vitamin C, and folic acid. This is partly due to the dearth of useful biomarkers used in studies cited (e.g. serum calcium was used in calcium fortification studies). Moreover, only 8 fortification studies were identified from

the scoping review, and numbers may be too few to make conclusive statements of whether fortification could improve micronutrient status.

Hypothesis 3: From the menu analysis, the hypothesis that LTC menus show variability and do not meet the RDA for several nutrients was supported, as large variations were seen in the menus for specific macro-and micronutrients, despite Homes using the Canada's Food Guide as a guideline for menu planning. This suggests that standards beyond the CFG should be in place to ensure consistency of nutrient provision between nursing homes. Different standards and regulations between provinces may be an issue. Thus, efforts can begin at a provincial level, with the goal of eventually improving LTC menu planning standards across Canada.

Hypothesis 4: From the acceptability testing, the hypothesis that micronutrient fortification will be an acceptable intervention for stakeholders, and be preferred over pill-form of micronutrient interventions was partially supported. Participants identified micronutrient fortification as a useful alternative, yet evidence of efficacy is needed to fully determine the acceptability of fortification. Moreover, a small number of participants also preferred ONS over fortification, as ONS was a simpler method that provided both micro-and macronutrients to residents. However, participants also agreed that micronutrients are a much less common topic of discussion between LTC providers, and less is known about micronutrients compared to macronutrients. This gap in knowledge of micronutrients amongst clinicians could be a reason why micronutrients do not receive much focus in LTC. This points to the need of changing both provider and resident/family's attitude towards micronutrients through knowledge translation efforts, to increase their understanding of physiological impact of micronutrient deficiencies on residents, and benefits of providing adequate micronutrients.

In summary, micronutrient malnutrition appears to exist in LTC when defined as inadequate intake, and biomarker status indicates that residents may be at risk of certain micronutrient deficiencies. Several strategies have been used to enhance resdients' micronutrient intake (and status), and micronutrient fortification of key food vehicles is an acceptable and potentially viable strategy for prevention of deficiency in residents living in LTC.

# 9.3 Proposed Micronutrient Fortification Strategy

Thus far, the thesis has identified micronutrients that may be candidates for a fortification formulation, based on diverse assessment methods. The micronutrients identified were: vitamins D (all sources), E (intake, menu analysis, super-menu), C (biomarker), B6 (intake), folate (intake, biomarker, menu analysis), calcium (intake, fortification studies), iron (biomarker) magnesium (menu analysis), and potassium (menu analysis, super-menu). Interestingly, most of these nutrients are Risk A or B nutrients, with iron as the only micronutrient in the Risk C category (see Background section, p. 18). This means that the majority of micronutrients either have a wide margin of safety with the UL, has no UL, or has non-serious critical adverse effects (Risk A nutrients); or has low risk of excessive intake at the proposed fortification level, i.e. up to 10% DV (Risk B nutrients) (89). Thus, addition of these nutrients to a fortification formula at physiological dosages (i.e. <50% RDA) or as regulation allows, is likely to be safe. The Linus Pauling Institute has developed older adult-specific micronutrient recommendations (65); recommendations that go beyond the RDA recommendations include: vitamin B12 at 100-400 mcg/day of crystalline supplemental vitamin B12 (due to malabsorption with age), vitamin D at 2,000 IU/day from supplements (due to reduced capacity for skin synthesis of vitamin D), and vitamin E: 200 IU of supplement of natural-source d-alpha-tocopherol (this dose is related to

protection from chronic diseases). The Linus Pauling Institute also cautions against supplementation of magnesium >350mg/d (due to prevalence of reduced kidney function in older adults, and to avoid risks of gastrointestinal disturbance) (65).

Several issues need to be addressed prior to pursuing micronutrient food fortification in LTC. Dosage levels trialed would need to take the regulations above into account, and be planned to the DRIs which provides a guideline to the needs of most in the population, and effort needs to be taken to ensure that the total daily averages consumed does not exceed the tolerable upper limit to avoid risk of toxicity.

From acceptability testing results, the selected food vehicle would be a food that is consumed well by the majority of residents. Based on these results, an outsourced product that was ready to consume was preferred, as it limited issues with error and staff time and negated the need for extensive training. Thus products for inclusion should include those that are readily outsourced. Furthermore, the amount to be eaten should be small to ensure full servings are consumed to enhance micronutrient intake and as per prior work, two offerings per day is reasonable to limit the effect of a missed meal or refused food item (112,119). Possible considerations include condiments (e.g. coffee creamers, butter/margarine), garnishes (e.g. whipped dessert topping), common sides (e.g. mashed potatoes), or soups. Regular textured foods would be trialed first, as additions to regular foods is likely the most simple. However, specific trialing and preparation processes with pureed would be also be needed, as simple additions of spices during cooking vs. during pureeing, have shown differences in sensory profiles (353).

If fortification is to occur with in-home production rather than outsourced, implementation could begin as a pilot in smaller homes (e.g. 100 resident or less) to allow better

control of and fidelity to fortification procedures, documentation and troubleshooting of barriers, and tracking of outcomes (354). Larger homes with larger production kitchens could be trialed in subsequent phases. Baseline micronutrient biomarker status data of participants should be collected, with regular tracking of intake (e.g. along with intake flowsheets, adding in a column to specify consumption of the fortified food item), and intermittent biomarker measurements should be taken depending on the micronutrient added and the half-lives of micronutrients in circulation. Effort should be taken to ensure that selected biomarkers are useful measures of micronutrient status (i.e. are sensitive and reliable).

Lastly, involvement with stakeholders at the start and throughout the potential fortification project is essential to ensure adherence and long-term success (121). Conducting focus groups or information sessions with resident/family and staff may help improve their understanding of the importance and reasons for fortification and encourage stakeholder buy-in. Marketing strategies, such as advertisements (e.g. posters, commercials), could help make the strategy more appealing to end users through repetition (355). Feedback from stakeholders (family/resident, LTC staff, government (for funding and to clarify regulations or develop new regulations as needed), and the research team) is also needed throughout the project to allow for changes to the strategy as needed.

It is the hope of the research candidate that the findings and suggestions of this thesis would not only provide insights into the barriers and challenges to enhancing residents' micronutrient intake and status, but also provide a taste of the benefits this work could bring if properly planned and executed.

## 9. 4 Study Strengths

Strengths of specific studies have been addressed in manuscripts (Chapters 5-8). Strengths of the overarching thesis included the use of triangulation at several levels, where the complementary strengths and non-overlapping weaknesses of each study component helped to address different areas of the research objective.

*Data trianglation* is where different sources of data are used to enhance validity (182). Data triangulation was achieved by incorporating literature reviews, menu analyses, and stakeholders' perespectives on micronutrient deficiencies in LTC, and whether a food fortification strategy might be feasible and acceptable in LTC from both the literature and stakeholders.

*Investigator triangulation* is when multiple researchers from the same field are involved in the study's analysis (182). This was done in the thesis by having more than one moderator conduct focus groups and key informant interviews and debriefing to discuss impressions after each data collection session. The use of multiple analysts independently coding transcripts and confirming and reducing emerging themes also allowed for further triangulation, increasing the authors' confidence of findings and helped establish the study's validity. Other researchers also confirmed SR selection of citations and extraction. Furthermore, a multidisciplinary thesis committee supported the work of the candidate ensuring that various perspectives from food and nutritional science and dietetics were represented in the data collection and interpretation.

*Theory triangulation* uses multiple perspectives outside the field to interpret available data (182). For this thesis, investigator triangulation occurred with the collaboration of committee members who were experts in different fields: dietetics, geriatrics, food science, and biochemistry. This helped inform all components of the study and encouraged critical analysis of

the results. For instance, while the research candidate and senior author identified that certain micronutrients were cited more frequently in the literature than others, and wondered if these were then the micronutrients of greatest concern, another committee member questioned whether frequency of citations truly indicated importance or just trends in research. This then resulted in focusing the SR results to examine consistency across studies, rather than simply frequency of micronutrients being studied, and noting that absence of research does not necessarily relate to adequacy of the nutrient.

Finally, *methodological triangulation* involves using two or more methods of data collection. This study was strengthend by using scoping reviews; menu analyses; focus groups or interviews with LTC staff, residents, and family members; and feedback questionnaires, which built on the development of subsequent stages. Each method then independently and later, collectively, answered its specific and the overall thesis research objective, and allowed for deeper understanding of which were the micronutrients for which residents may be at risk of deficiencies, and identified that food fortification was an acceptable strategy in LTC, given proof of concept and ease of application for LTC.

#### 9.5 Study Limitations

A considerable limitation of this study includes the heterogeneity of data, with varing levels of quality and accuracy. From the scoping reviews, identified intake studies of various diet assessment quality included (ordered from lesser to more accurate): diet histories, food frequency questionnaires, estimated food records, and weighed food records. Furthermore, some studies focused on high risk groups in LTC and not the overall population, affecting interpretation. Moreover, appropriateness of biomarkers were also of concern; micronutrient

statuses were examined with a variety of biomarkers of varying accuracy, ranging from highly useful (e.g. 25(OH)D) to less useful with some still inclusive in their utility to assess dietary exposure. Other biomarkers measured are tightly regulated, non-specific to the micronutrient, or old biomarkers that are no longer used in practice (39,56). This study did not aim to determine a direct relationship between intake and status, yet this is needed to demonstrate the efficacy of micronutrient-enhancing strategies.

Regarding menu analysis, only a small sample size (n=5) of Canadian LTC menus were used. Thus, this is not a sufficient analysis to fully characterize Canadian LTC menus, although it is more comprehensive that studies to date (5,48,70). Conclusions on the sufficiency or potential regional differences in menu planning cannot be made without a more comprehensive analysis.

Cost of super-menus was not established from this study, and it cannot be determined whether these menus are feasible under current LTC food budgets. Super-menus have also not been trialed in LTC homes, thus level of acceptance and compliance with consumption cannot be determined in this thesis. However, work is underway to trial fortification formulations identified from the scoping review with food vehicles of commonly consumed foods identified by the acceptability testing from this study. This will first be tested with professional taste-testers to address issues with taste changes, texture, and overall food appearance. By addressing these issues prior to implementation, it is hoped that higher acceptance could be obtained when trialing occurs with actual LTC residents in the future.

Intrinsic to the concept of food fortification is that the strategy will address micronutrient needs for the population in general, yet individual needs (e.g. due to disease states or other physiological limitations) may not be addressed. However, the concept and purpose of food fortification in LTC was that of prevention, with the recognition that any improvement in intake

and status may decrease the risk of deficiencies or maintain current status and help residents avoid the damaging effects of micronutrient malnutrition.

### 9.6 Future Research Directions and Implications for Practice

This work was exploratory, and certain areas require greater attention in future studies. Due to the diversity in study designs identified in the scoping reviews, comparisons of efficacy within supplementation and fortification, and between the two strategies, were difficult. Future studies examining the effects of supplementation or fortification with a LTC-specific micronutrient formulation should consider measuring both intake and resulting biomarker status changes to comment on possible relationships between intake and status. Biomarkers of function may also be considered for examination, as changes in function provides stronger evidence for the benefits of adequate micronutrient intake (39,313). Length of the study should be determined after considering the number of days required to adequately assess micronutrient intake, as recommended by Bingham (1987).

### **Population to Target**

To demonstrate efficacy of fortification, a long-term efficacy study measuring intake, status, and even functional changes after intake of micronutrients would be ideal. However, this type of study may be difficult to carry out with the current LTC populaton. While life expectancies for older adults have been reported to increase (4,356,357), those admitted to LTC remain an ill population that live with comorbidities (358,359), and risk of mortality following placement in LTC remains high (360–362). Thus, the feasibility of a long-term study is a limitation with this population. Disease states may also confound the precision and accuracy of biomarkers used (39). Beginning research with the retirement population may allow for a longer

period of follow-up, but the retirement population is not well-defined, and range of health, eating habits, and functional abilities may make comparisons difficult. As follows, identification of an older adult population for which micronutrient fortification can be carried out for an appropriate length of time to demonstrate its efficacy at improving micronutrient status is still needed.

#### **Future Directions for Micronutrient Provision in LTC**

For LTC practice, Homes should be equipped with micronutrient analysis programs (or have analyzed menus) to ensure that menus meet recommendations. Prior to fortification work, greater awareness of micronutrient contents of food can help improve menu planning. Having LTC facilities re-examine current menus to analyze micronutrient contents of the menus may be a first step. Identification and incorporation of micronutrient-dense foods on the menu can help to maximize residents' nutrient intake, and further work can be done to reduce food volume by including these nutrient-dense ingredients. Findings suggest that meeting most micronutrient recommendations is possible with creative and deliberate menu planning and knowledge translation of best practices is needed, as well as determining the potential cost of super-menus. To facilitate these objectives, stakeholders' understanding and buy-in, from the level of residents, to staff, to government support, are essential.

To advance micronutrient food fortification in LTC, taste-testing to address issues with taste changes, texture, and overall food appearance, as well as determination of stability with production and storage needs to be assessed and tested. This work is currently being done at the University of Guelph under Dr. Lisa Duizer in the Department of Food Science. Their findings will help answer issues noted by stakeholders and allow for better assessment of acceptability.

Piloting in LTC homes' production kitchen will allow for external validity or transferability, to assess whether this strategy is feasible in the daily LTC production kitchen.

Although this study was able to narrow down the micronutrients for which residents are at risk of deficiency, it was not possible to pinpoint a final list of micronutrients for which all LTC residents would benefit from. This study results from differrent levels of assessment and analyses (i.e. intake data, biomarker status, intervention formulations, menu analysis, and supermenu comparisons) which identified different micronutrients of concern. Vitamin D was the micronutrient that appeared across all studies, and can be assumed as a micronutrient which all residents may benefit from fortification, given its benefits on bone status and decreased skin synthesis with age (93,112,349). While the other micronutrients may be of concern, other considerations may render them inappropriate for supplementation and fortification. For instance, with iron, contraindications to supplementation (65) or issues with acceptability of the fortification (119) may mean it will not be considered in the potential micronutrient formulation. Of all the assessment methods used, micronutrient biomarkers are likely the most precise measurement. However, micronutrient requirements may differ from nation by nation due to differences in fortification practices, cultural food intake patterns, food availability, and other factors. Thus, a nation-wide study of LTC residents' intake and biomarker status, specifically evaluating the micronutrients from the findings above, may be a logical next step to answering which are the micronutrients of concern that should be addressed in LTC.

# 9.7 Conclusion

This study has advanced the knowledge of micronutrients of concern in LTC through careful examination and comparison of current literature, and critically evaluated potential

strategies to enhance micronutrient status through review of literature and gathering of stakeholder and experts' perspectives. This is the first known study to examine the use of webinar focus group as a data collection method for research, and provided insight, guidance, and trouble-shooting advice for future webinar focus group designs. Triangulation of data, investigators, theory, and methods helped to address research objectives and the gap in understanding of the depth of micronutrient malnutrition and potential strategies to ameliorate this form of malnutrition for residents living in LTC. This thesis provides direction for where to address research efforts, as well as possible changes to practice needed for LTC. Given the recent interest in micronutrient fortification in LTC (112,115,119,298), and the increasing numbers of LTC residents in Canada (1) and worldwide (4), focus on micronutrient needs for LTC residents is a timely research endeavour.

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#### Appendices

#### Appendix A

#### UNIVERSITY OF WATERLOO

#### OFFICE OF RESEARCH ETHICS

#### Notification of Ethics Clearance of Application to Conduct Research with Human Participants

Faculty Supervisor: Heather Keller Student Investigator: Ivy Lam Collaborator: Ken Stark Collaborator: Lisa Duizer

Department: Kinesiology Department: Kinesiology Department: Kinesiology Department: University of Guelph

ORE File #: 18558

Project Title: Enhancing Food in Long-Term Care

This certificate provides confirmation that the additional information/revised materials requested for the above project have been reviewed and are considered acceptable in accordance with the University of Waterloo's Guidelines for Research with Human Participants and the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans. Thus, the project now has received ethics clearance.

Note 1: This ethics clearance from the Office of Research Ethics (ORE) is valid for one year from the date shown on the certificate and is renewable annually, for four consecutive years. Renewal is through completion and ethics clearance of the Annual Progress Report for Continuing Research (ORE Form 105). A new ORE Form 101 application must be submitted for a project continuing beyond five years.

Note 2: This project must be conducted according to the application description and revised materials for which ethics clearance has been granted. All subsequent modifications to the project also must receive prior ethics clearance (i.e., Request for Ethics Clearance of a Modification, ORE Form 104) through the Office of Research Ethics and must not begin until notification has been received by the investigators.

Note 3: Researchers must submit a Progress Report on Continuing Human Research Projects (ORE Form 105) annually for all ongoing research projects or on the completion of the project. The Office of Research Ethics sends the ORE Form 105 for a project to the Principal Investigator or Faculty Supervisor for completion. If ethics clearance of an ongoing project is not renewed and consequently expires, the Office of Research Ethics may be obliged to notify Research Finance for their action in accordance with university and funding agency regulations.

Note 4: Any unanticipated event involving a participant that adversely affected the participant(s) must be reported immediately (i.e., within 1 business day of becoming aware of the event) to the ORE using ORE Form 106.

IAA1 Maureen Nummelin, PhD

Director, Office of Research Ethics

OR Susanne Santi, MMath Senior Manager, Research Ethics

OR Julie Joza, MPH Manager, Research Ethics

6/2012

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## Appendix B

## Webinar invitation letter – Dietitians of Canada Example

Dear [name of Registered Dietitian], Here is an opportunity to participate in a LTC food fortification study. See the details and contact information below.

Debra McLennan, RD Chair, Gerontology Network

## Faculty of Applied Health Sciences Department of Kinesiology University of Waterloo PARTICIPANTS NEEDED FOR RESEARCH IN "ENHANCING FOOD IN LONG-TERM CARE"

#### WHO: Nutrition Managers, Chefs and Dietitians in Long-Term Care

**WHAT**: We would like to invite you to take part in a webinar to discuss how to improve the nutrient quality of food provided to long-term care residents in Canada. One strategy is to fortify the food with vitamins and minerals. As staff in a long-term care home, you have unique understandings relating to issues, challenges, and strategies to improve your residents' food intake. We are interested in hearing your opinions on this specific strategy of fortifying key food products.

**HOW:** As a participant in this study, you would be asked to provide your insights and opinions on fortification of food products during a webinar focus group with other long-term care personnel. Participation requires a computer with internet access and a phone line.

Your participation would involve one 45-minute session.

**WHY:** Your participation will help us to determine if food fortification is an acceptable and feasible strategy to improve nutrient intake of residents. For more information about this study, or to volunteer for this study, please contact:

Ivy Lam, BASc MSc Candidate, Dept. Kinesiology University of Waterloo Email: <u>ivy.lam@uwaterloo.ca</u>

This study has been reviewed by, and received ethics clearance through, the Office of Research Ethics, University of Waterloo.

## Appendix C

#### Webinar Pre-Session Registration Survey

#### **Enhancing Food in Long Term Care**

Thank you for your interest in our webinar to discuss how to improve the nutrient quality of food provided to long-term care residents in Canada. As a participant in this study, you will be asked to provide your insights and opinions on vitamin and mineral fortification of food products during a webinar focus group with other long-term care personnel. Participation requires a computer with internet access and a phone line.

\* Required

- 1. Full Name \*\_\_\_\_\_
- 2. Email address \*\_\_\_\_\_
- 3. Phone number (The number we will be contacting you at) \*\_\_\_\_\_
- 4. Which city and province do you work in? (This will give us a better understanding of different time zones and help us with the grouping assignment of the webinars. (e.g. Toronto, ON)) \* \_\_\_\_\_\_
- 5. What is your current work position? \*
- Registered Dietitian
- Nutrition Manager
- Chef
- Other\_\_\_\_\_
- 6. How long have you been working in Long Term Care? \*
- Less than 1 year
- 1-5 years
- 5 10 years
- 10 15 years
- >15 years
- 7. Webinar dates: (Please pick THREE) \*

You are only required to attend ONE webinar. Please note: 11-12 pm EST (e.g. Ontario) = 8-9 am PST (e.g. BC) = 9-10 am MST (e.g. AB) = 10-11am CST (e.g. MB) [LIST OF SESSION DATES]

- 8. If none of the times above work for you, please list additional date(s) and time(s) that you would prefer:
- 9. Will anyone else be joining you in the webinar?

10. Please list their name(s) and position(s). (E.g. Ivy Lam, Registered Dietitian) 11. Comments?

## Appendix D

#### Webinar Outline and Discussion Questions



200 University Avenue West, Waterloo, ON, Canada, N2L 3G1 519-888-4567 | uwaterloo.ca

# Enhancing Food in Long-Term Care

#### Webinar Outline and Discussion Questions

The purpose of this focus group webinar is to examine the feasibility of micronutrient (MN) fortification of food in Long-Term Care (LTC). Specifically, we are interested in learning from LTC providers: 1) what mutrients you are concerned about for your residents; what foods are most poorly consumed, 2) how the LTC home is currently attempting to meet nutritional needs specific to micronutrients, 3) your thoughts on fortification of key food products as a potential strategy, and 4) any concerns (e.g. stability, safety, regulations) you may have with this strategy.

#### Process:

Webinars will be used for these focus groups (FG) webinars. Sessions are also automatically audio-recorded. By signing up for and attending a webinar, this will imply your consent for the study and for audio-recording. FG will be ~45 minutes in length. The FG will be held online with 4-6 participants (i.e. LTC Chefs, Dietitians, Nutrition Managers) per group. Participants will be provided with an online powerpoint presentation on *micronutrient enhancement of food in long-term care homes*, and be asked to discuss your views throughout the FG.

#### Before Focus Group:

- An e-mail will be sent with instructions on how to sign on to the webinar, along with a confirmation of the time you've signed up for, the call-in number and the webinar event password. Please also read over the discussion questions below to prepare for FG
- 2) Reminder e-mails will be sent to participants two week days prior to the webinar. You may have to install the meeting application before the webinar, so we recommend that you install it after you receive the reminder e-mail to ensure you have no trouble with attending the webinar.
- If you cannot attend a webinar, please let us know immediately (email ivy.lam@uwaterloo.ca), and we will arrange for you to attend another webinar.
- Please call/sign in 10-15 minutes before the webinar begins to make sure we begin on time.

#### At the Focus Group:

- We will give a reminder that this is a research focus group and that comments will be recorded and kept confidential. The format of the FG webinar includes both group discussions and online polling. We will discuss the process for online polling.
- 2) We will also answer any questions about focus groups or process before we begin.

#### After the Focus Group:

 Participants will be emailed a link to the feedback form to provide comments on webinar information, experience, and other suggestions. WATERLOO

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# Webinar Questions

#### Introduction

Prevalence of micronutrient malnutrition in Long-term care (LTC)

- 1. What are key foods that are poorly consumed?
- 2. What are foods almost all residents will consume?
- 3. We found that certain nutrients (e.g. calcium, zinc, and vitamins C, D, thiamine, riboflavin, niacin, B6, folate, and B12) were low in older adults' food consumption, and we usually find these nutrients in these foods (list of foods). What is the consumption rates of these foods in your LTC home?
- 4. What evidence do you have that specific nutrients are a problem in your residents? a. Is there screening process?
- 5. What do you currently do to try to meet these micronutrient needs?

#### Presentation of Data

One of the strategies to improve micronutrient status is micronutrient fortification. Present results from recent Canadian studies on food intake in LTC

Adolf 2009 - Vitamin Fortification of Pureed Foods For Long-term Care Residents

Mocanu et al, 2009 – Long-term effects of giving nursing home residents bread fortified with125 µg (5000 IU) vitamin D3 per daily serving)

- 5. What are your concerns with micronutrient food fortification?
- 6. What foods would be good food vehicles for fortification?

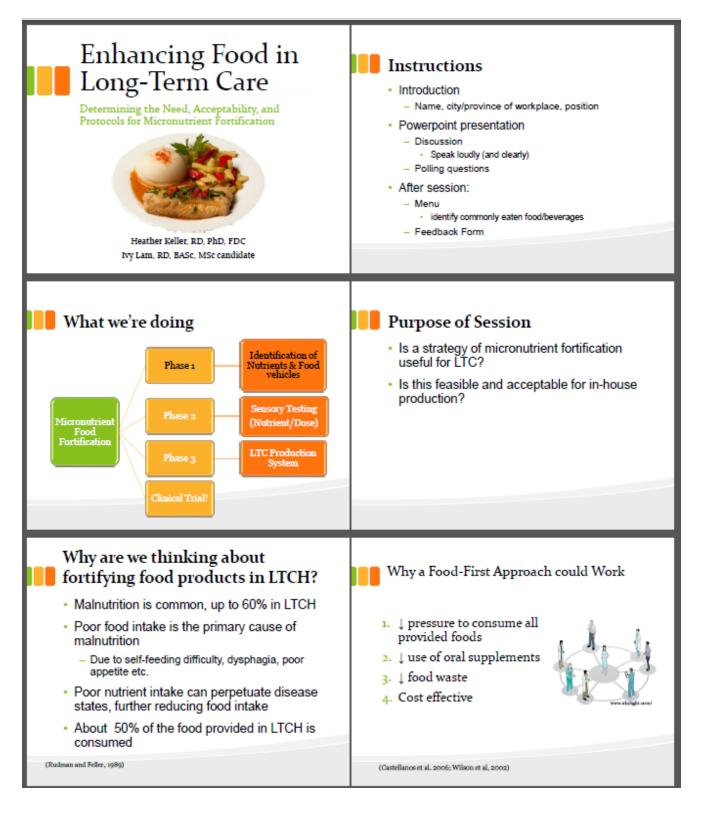
#### Strategies for fortification

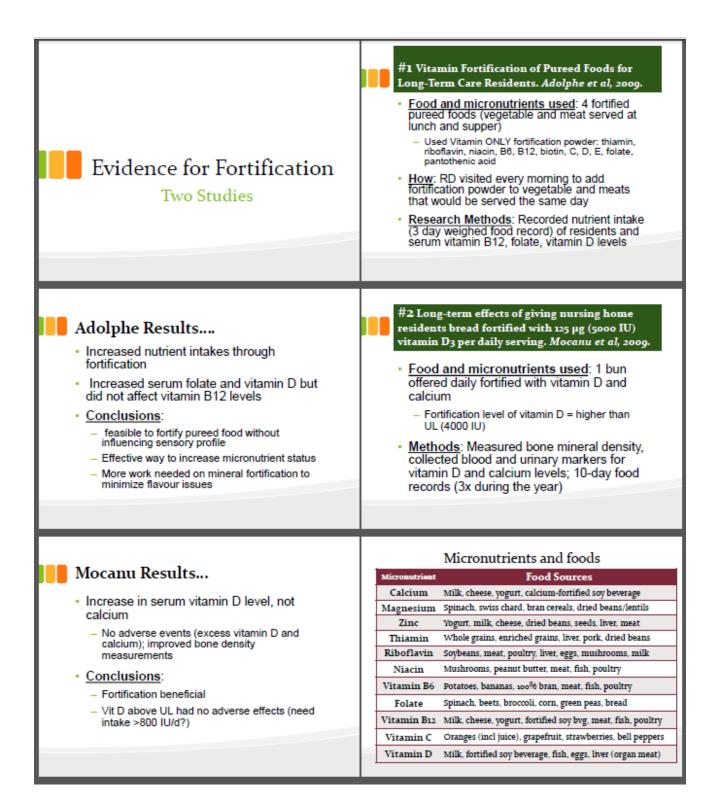
- 7. What would be the challenges for fortification in your home?
  - a. How much/What percentage of your home's food budget is currently spent on nutritional supplements (e.g. Ensure)?
  - b. With the increased food budget starting in January 2013 to \$7.68, how much are you likely to spend on supplements?
- 8. How can you see this being incorporated in your home's production.
  - e.g. stability, taste, safety, regulations
  - Talk about potential production issues
- 9. What are some strategies you would consider in addressing these issues/concerns?

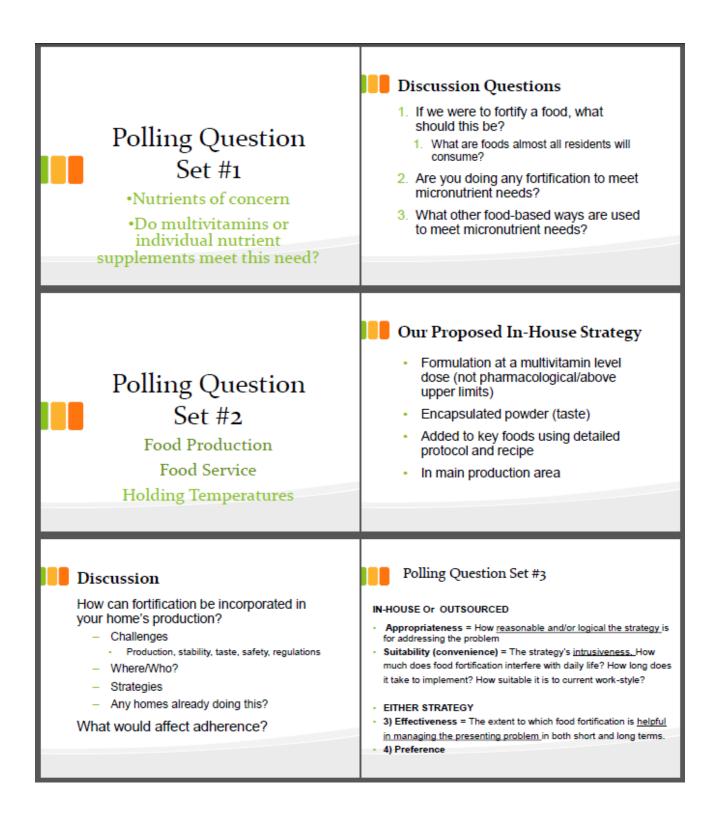
By: Ivy Lam, RD, BASc, MSc student Please contact Ivy (ivy.lam@uwaterloo.ca) if you have any questions regarding this study.

## Appendix E

#### Webinar PowerPoint Presentation







## Appendix F

## Webinar Feedback Form

## Feedback Form: Enhancing Food in Long-Term Care

We would like to thank you for your participation in the Enhancing Food in Long-Term Care webinar focus group (determining the need, acceptability, and protocols for micronutrient food fortification). As a reminder, the purpose of this study was to address the complex issue of micronutrient malnutrition through determining the feasibility of micronutrient fortification of food in long-term care.

\* Required

I am	а	*
------	---	---

О Chef 0

- o <sup>O</sup> Dietitian
- • Nutrition Manager
- Other:

Please tell us which city AND province you work in. \*

## **Overall Webinar**

Please rate how much you agree with the following statement: The webinar was what I had expected. \*

Checkbox option: 1 (completely disagree) to 5 (completely agree)

If it did not meet your expectations, how can we improve the webinar so that it would meet your expectations? If it exceeded your expectations, please also explain.

Your response will help us improve future sessions. Thank you.

*During the webinar, how much of the INFORMATION PRESENTED were you able to understand?* \* Checkbox option: 1 (none of it) to 5 (all of it)

*During the webinar, how much of the DISCUSSION were you able to understand? \** Checkbox option: 1 (none of it) to 5 (all of it)

What would help improve the understandability of the INFORMATION PRESENTED?

	The	e length of time (1 hour) for this webinar was *
0	0	Too short
0	0	Just right
0	0	Too long
	(If	ommunicated as much as I had wanted to in the webinar.* you select "No," please ALSO use the "other" section to provide an lanation)
0		Yes
0	$\Box$	No
0	□ The	Other: group was given enough time for discussion. *
0		Yes
0		No
0		Other:
	$\cap$	e size of the group (4-6 participants) was *
0	_	Too small
0	0	Just right
0	0	Too large

## Using WebEx - Online Focus Groups

Next, we want to learn more about your experience in using the online focus group format. I found the WebEx (webinar) program easy to use \*  $^{\circ}$ Yes 0  $\bigcirc$ No 0  $^{\circ}$ Somewhat 0 It took me \_\_\_\_\_\_ minutes to sign on to the webinar session. \* О <5 minutes 0 O 5 - 10 minutes 0 0 >10 minutes 0 *The information I was sent before the webinar was* \_\_\_\_\_\_ *to prepare* me for the webinar focus group.\* О Not enough 0  $^{\circ}$ Just enough 0 О Too much 0

Please rate the following on a scale of 1 to 5: (1=strongly agree; 5 = strongly disagree)

> *It was easy to sign on to the webinar.* \* Checkbox option: 1=strongly disagree; 5 = strongly agree

> *It was easy to use the webinar program.* \* Checkbox option: 1=strongly disagree; 5 = strongly agree

*I had no problem hearing THE FACILITATOR in the webinar.* \* Checkbox option: 1=strongly disagree; 5 = strongly agree

*I had no problem hearing OTHER PARTICIPANTS in the webinar.* \* Checkbox option: 1=strongly disagree; 5 = strongly agree

Compared to an in-person focus group, the online focus group was

• • Better

\*

- • Worse
- $_{\circ}$  The same

I would recommend online webinar focus groups for this type of research. \*

- ° Yes
- 。 <sup>0</sup> No
- • Not sure

## **Final suggestions**

(Almost there. Thank you for your patience.) *What did you like about this session?* 

What could we have done to improve this session for you? How can we improve sessions for future attendees?

What was the most valuable thing you learned from the webinar (presentation, polling questions, and/or group discussion)?

I would have liked to learn more about \_\_\_\_\_\_.

Additional comments

## Appendix G

## Participant Feedback/Thank You Letter: Webinar Example

Dear Nutrition Managers, Chefs and Dietitians in Long-Term Care:

We would like to thank you for your participation in this study entitled Enhancing Food in Long-Term Care. As a reminder, the purpose of this study was to address the complex issue of micronutrient malnutrition through determining the feasibility of micronutrient enhancement of food in long-term care. Over the next few months, we will continue to hold focus groups with long-term care personnel to explore the issues, challenges, concerns, and potential strategies for fortification of food products in LTC.

Please remember that any data pertaining to you as an individual participant will be kept confidential. Once all the data are collected and analyzed for this project, we plan on sharing this information with the research community through seminars, conferences, presentations, and journal articles. If you are interested in receiving a summary of the results, please provide your email address. We anticipate completion of data collection by December 2013 and an executive summary will be available early in 2014. In the meantime, if you have any questions about the study, please do not hesitate to contact **Ivy** or **Professor Heather Kelle**r by email or telephone as noted below. As with all University of Waterloo projects involving human participants, this project was reviewed by, and received ethics clearance through, the Office of Research Ethics at the University of Waterloo. Should you have any comments or concerns resulting from your participation in this study, please contact Dr. Maureen Nummelin, the Director, Office of Research Ethics, at 1-519-888-4567, Ext. 36005 or <u>maureen.nummelin@uwaterloo.ca</u>.

Yours truly

Ivy Lam RD, BASc MSc Candidate, Dept. Kinesiology (Physiology and Nutrition) University of Waterloo ivy.lam@uwaterloo.ca

Heather Keller RD, PhD, FDC Professor, Schlegel Research Chair, Nutrition & Aging Dept. Kinesiology University of Waterloo 519 888-4567 (x 31761) hkeller@uwaterloo.ca

#### Appendix H

#### Key Informant Info Letter



Kinesiology – Physiology and Nutrition University of Waterloo 200 University Avenue West Waterloo, Ontario, Canada N2L 3G1

#### Enhancing Food in Long-Term Care

We would like to invite you to participate in a telephone interview on how to improve the nutrient quality of food provided to long-term care residents in Ontario. As a MSc student in the Faculty of Applied Health Sciences at the University of Waterloo, I am currently conducting this research under the supervision of Professor Heather Keller.

#### Why is it important to get your input

Micronutrient deficiency is prevalent among older adults living in long-term care, affecting functional ability, cognition, and quality of life. A varied diet is needed to meet nutrient requirements, but changes with age lead to decreased food intake and put older adults at increased risk of nutrient deficiencies. Improving food quality through micronutrient enhancement may allow residents to meet nutrient requirements through foods they like and already consume. This strategy would provide the required nutrition in a smaller amount of food, leading to reduced use of oral supplements and less food waste.

We need your input to determine the acceptability and feasibility of micronutrient enhancement of food in long-term care. Specifically, we are interested in learning about: 1) what is currently done in long-term care homes in attempt to meet specific micronutrient needs, 2) what are the potential issues (e.g. stability, safety, regulations) to be considered when fortifying foods in long-term care, and 3) your opinion on the utility of fortification of key food products as a potential strategy. This study is the first of its kind, taking an innovative approach to address micronutrient malnutrition in long-term care. Data collected will be used to further develop this strategy.

#### What does this study involve

You are being asked to participate in a key informant interview conducted by telephone. The interview will last approximately 45 minutes and would be arranged at a time convenient to your schedule. The interview will be conducted by Professor Heather Keller (I will sit in as a note-taker and co-moderator) and it will be audio recorded with your permission.

#### What your participation means

Participation in the interview is entirely voluntary and there are no known or anticipated risks to participation in this study. Attending the interview will imply your consent to participate in this research study. Sessions will be audio recorded to ensure the accuracy of your input, and transcribed. All information you provide will be considered confidential and grouped with responses from other participants. Only first names will be used during the call and will be removed from the transcript. Specific comments you make will not be linked to your name in transcripts. Furthermore, you will not be identified by name in any report or manuscript resulting from this research. With your permission, anonymous quotations may be used in publications.

#### Key Informant Info Letter

You may decline to answer any of the questions you do not wish to answer. Furthermore, you may decide to withdraw from this study at any time, without any negative consequences. All information you provide will be considered confidential and the data collected will be kept in a secure location and confidentially disposed of in five years time at the *University of Waterloo*.

Contact Information

If you have any questions regarding this study, or would like additional information about participation, please contact me by email *ivy.lam@uwaterloo.ca*. You can also contact my supervisor Professor Heather Keller by telephone at 1-519-888-4567 ext. 31761 or by email at *hkeller@uwaterloo.ca*. If you are interested in receiving a copy of the executive summary of the session outcomes, please contact *Professor Heather Keller* at <u>hkeller@uwaterloo.ca</u>.

This study has been reviewed and received ethics clearance through the Office of Research Ethics at the University of Waterloo. If you have any comments or concerns resulting from you participation in this study, please contact Dr. Maureen Nummelin in the Office of Research Ethics at 1-519-888-4567, Ext. 36005 or <u>maureen nummelin@uwaterloo.ca</u>.

Thank you in advance for your interest and assistance with this research.

Sincerely,

Heather Keller, RD PhD FDC Schlegel Research Chair Nutrition & Aging, Dept. Kinesiology

> Ivy Lam, RD MSc Candidate, Dept. Kinesiology

This study has been reviewed by, and received ethics clearance through, the Office of Research Ethics, University of Waterloo.

## Appendix I

## **Key Informant Interview Outline and Questions**

Key Informant Interview Questions



Kinesiology – Physiology and University of Waterloo Nutrition

University of Waterloo 519 888-4567 (x 31761) 200 University Avenue West Waterloo. Catalog. Canada Waterloo, Ontario, Canada N2L 3G1

# Enhancing Food in Long-Term Care

#### Key Informant Interview Process & Questions

Thank you for participating in the Enhancing Food in LTC webinars a few weeks ago. The webinars provided us with an overview of opinions on the strategy of food fortification in LTC. We have begun to analyze the data and recognize the need for a bit more in-depth information from a few individuals who have a unique understanding relating to issues and potential challenges with this strategy.

We would like to invite you to take part in a one-on-one key informant interview to explore in greater depth the strategy of fortification.

#### Process:

Key informant interviews will be conducted over the phone, and will last about an 45 minutes.

#### Before the Interview:

1) You will receive reminder e-mails one week, and again one day, prior to the interview.

#### **During the Interview:**

- You will be reminded that this is research interview and that comments will be recorded and amalgamated with other interviews and focus groups conducted with LTC staff
- 2) Professor Heather Keller will lead the interview, with Ivy as the note-taker and co-moderator.

Enhancing Food in Long-Term Care | 1

#### Key Informant Interview Questions

#### Key Informant Interview Questions

1. What are your concerns with adequacy of food intake in LTC in Ontario?

2. From your perspective, what are the key limiting factors with respect to food products that influence the adequacy of the diet of LTC residents?

One of the strategies to improve micronutrient intake and nutritional status in LTC is micronutrient fortification [the proposed strategy will be further described]

3. What do you think of this strategy for improving micronutrient intake for LTC residents?

4. What are your concerns?

5. What do you see as barriers to fortification?

6. From your perspective, would facilities accept this strategy? What would facilitate uptake of this strategy?

Please e-mail Ivy Lam (<u>ivy.lam@uwaterloo.ca</u>) to provide your available times for the interview.

Thanks for your time.

Sincerely,

Heather Keller, RD PhD FDC Schlegel Research Chair Nutrition & Aging, Dept. Kinesiology

> Ivy Lam, RD MSc Candidate, Dept. Kinesiology

This study has been reviewed by, and received ethics clearance through, the Office of Research Ethics, University of Waterloo.

Enhancing Food in Long-Term Care | 2

## Appendix J

## **Resident/Family Focus Group Information Letter**



Kinesiology – Physiology

and Nutrition

200 University Avenue West Waterloo, Ontario, Canada

University of Waterloo

519 888-4567, 31761 hkeller@uwaterloo.ca

# Dear Food Committee attendee,

This letter is an invitation to participate in a research study. As a MSc. student Applied Health Sciences at the University of Waterloo, I am currently conducting research under the supervision of Professor Heather Keller on micronutrient enhancement of food in long-term care homes.

Nutrient deficiency is a prevalent but preventable problem among older adults living in long-term care. Inadequate intake of nutrients affects function, cognition, and quality of life. A varied diet is needed to meet nutrient requirements, but changes with age affect taste, appetite, and nutrient use by the body, leading to an increased likelihood of insufficient nutrition. Improving food quality through nutrient enhancement of regular food may allow older adults to meet nutrient requirements through foods rather than pills or liquid supplements.

The purpose of this group discussion at your Food Committee is to examine the feasibility of nutrient fortification of food in long term care and retirement homes. Focus groups and key informant interviews have already been done with long term care staff (dietitians, nutrition managers, chefs) to determine their opinion about enhancing foods. The opinion of residents and/or their families is important to ensure that we also understand your perspective. Our intent is to use the open forum discussion of the Food Committee to present this strategy for improving nutrition of residents and identify any concerns you may have with this strategy.

Discussion will occur in the open forum of the Food Committee. We will take notes of your comments and discussion points. As well, we will leave you with a one-page feedback form where you can anonymously provide any further comments. Being present in the Food Committee meeting does not mean that you must participate in the discussion or provide a feedback form. Your name and the name of your organization will not appear in any thesis or publication resulting from this study. If you have any questions regarding this study, or would like additional information about participation or the results, please contact my supervisor Professor Heather Keller by telephone at 1-519-888-4567 ext. 31761 or by email at <u>hkeller@uwaterloo.ca</u>.

This study has been reviewed and received ethics clearance through the Office of Research Ethics at the University of Waterloo. If you have any comments or concerns about this study, please contact Dr. Maureen Nummelin in the Office of Research Ethics at 1-519-888-4567, Ext. 36005 or <u>maureen.nummelin@uwaterloo.ca</u>. Thank you in advance for your interest and assistance with this research.

Yours very truly,

Ivy Lam RD, MSc Candidate

## Appendix K

## Family/Resident Focus Group Consent Form

# Agreement to participate

By signing this consent form, you are not waiving your legal rights or releasing the investigator(s) or involved institution(s) from their legal and professional responsibilities.

I have read the information letter about the **micronutrient enhancement** of food in long term care study under the supervision of Professor Heather Keller at the University of Waterloo. I have had an opportunity to ask any questions related to this study, to receive satisfactory answers to my questions, and any additional details I wanted.

I was informed that I may withdraw my consent at any time without penalty by advising the researcher.

By providing your signature below, I provide my consent to participate in this study.

Print Name

Signature

Date

Witness

## Appendix L

Family/Resident Focus Group Question Outline and Feedback Questionnaire

# Enhancing Food in Long-Term Care

# **Food Committee Focus Group Discussion Questions**

- 1. Are you concerned that some residents do not get enough nutrition from the food they eat?
- 2. What do you think of this strategy for adding nutrients to food products consumed by most residents? Probe: concerns about safety, quality of food, 'doctroing up' food etc.

# Food Committee Feedback Form

- 1. On a scale of 1(not at all) to 5 (very much so) how acceptable to you is the strategy of adding nutrients to regular food to improve the nutrition of residents in long term care? (Please check ONE of the boxes below)
  - $\Box$  1 (Not at all)
  - □ 2
  - □ 3
  - □ 4
  - $\Box$  5 (Very much so)
- 2. What do you like about this strategy?
- 3. What are your concerns with this strategy?

## TABLES

	Table 1. Database Search Terms
Database	Search Terms
	<ul> <li><u>Subject Headings</u></li> <li>1. Exp food, fortified/ OR exp foods, specialized/ OR eating/ OR nutrition therapy/ OR diet therapy/ OR food analysis/</li> </ul>
	<ol> <li>long-term care/ OR exp residential facilities/ OR exp nursing home/ Note:</li> </ol>
	<ul> <li>EXPLODE Foods, specialized (includes: food, fortified AND food, formulated AND functional food AND health food);</li> </ul>
	<ul> <li>EXP food, fortified (includes prebiotics)</li> <li>EXP dietary supplements (incl: prebiotics, probiotics, synbiotics, yeast)</li> <li>EXP eating (incl: drinking, mastication)</li> </ul>
	• EXP residential Facilities (incl: assisted living facilities, group homes, homes for the aged)
Medline – OVID	EXP nursing homes (incl: intermediate care facilities, skilled nursing facilities)  Author Key words
	<ol> <li>(Fortified adj2 food\$).tw. OR (food fortif\$).tw. OR eating.tw. OR (food\$ adj2 intake\$).tw. OR (oral\$ adj2 intake\$).tw. OR ((food\$ or meal\$ or drink\$ or beverage\$ or diet\$ or snack\$ or breakfast\$ or break-fast\$ or lunch\$ or dinner\$) adj5 (fortif\$ or enrich\$ or supplement\$)).tw. OR (food\$ adj2 enhance\$).tw.</li> <li>(long term care\$ or long-term care\$ or nursing home\$ or retirement home\$</li> </ol>
Medline - OVID	or residential facilit\$).tw. OR (geriatric adj2 (home\$ or unit\$ or facilit\$ or institution\$)).tw.
	Subject Headings
	<ol> <li>MH Food, fortified OR MH food, formulated OR MH dietary supplements+ OR MH food analysis OR MH eating OR MH food intake</li> <li>MH long term care OR MH residential care OR MH nursing home patients OR nursing homes+ OR residential facilities</li> </ol>
	Note:
	<ul> <li>Food, fortified (already at end of tree)</li> </ul>
	<ul> <li>Food, formulated (+ includes infant formula, but one article used infant formula for older adults)</li> </ul>
CINAHL	<ul> <li>Not (+) residential care b/c incl respite care</li> <li>Nursing home+ incl skilled nursing facilities</li> </ul>
	<ul> <li>Author Key words</li> <li>1. TI fortified food* OR AB fortified food* OR TI food fortif* OR AB food fortif*</li> </ul>
	<ol> <li>Thiortified food "OR AB fortified food" OR Thiod fortif" OR AB food fortif OR TI eating OR AB eating OR TI food* intake* OR AB food* intake* OR TI oral* intake* OR AB oral* intake* OR MH food, fortified OR MH food, formulated OR MH "dietary supplements+" OR MH food analysis OR MH eating OR MH food intake OR TI food enrich* OR AB food enrich* OR TI meal supplement* OR AB meal supplement* OR TI diet fortif* OR AB diet fortif* OR TI diet enrich* OR AB diet enrich* OR TI food* enhance* OR AB food* enhance*</li> <li>TI long term care OR AB long term care OR TI long-term care OR AB long-term care OR AB retirement home* OR TI residential facilit* OR AB residential facilit* OR MH long term care OR MH residential care OR</li> </ol>
	MH nursing home patients OR MH "nursing homes+" OR MH
CINAHL	residential facilities OR TI geriatric home* OR AB geriatric home* OR TI

## Table 1. Database Search Terms

	geriatric unit* OR AB geriatric unit* OR TI geriatric facilit* OR AB geriatric
	facilit* OR TI geriatric institution* OR AB geriatric institution*
Web of Science	Subject Headings Not applicable
	Author Key words 1. TS=(eating) OR TI=(eating) OR TI=((food intake*)) OR TS=((food intake*)) OR TI=((oral intake*)) OR TS=((oral intake*)) OR TI=((food fortif*)) OR TS=((food fortif*)) OR TI=((fortified food*)) OR TS=((fortified food*)) OR TS=((food* enhance*)) OR TI=((food* enhance*))
Web of Science	<ol> <li>TS=((long-term care*)) OR TI=((long-term care*)) OR TI=((nursing home*)) OR TS=((nursing home*)) OR TI=((long term care*)) OR TS=((long term care*)) OR TS=((residential facilit*)) OR TI=((residential facilit*)) OR TS=((retirement home*)) OR TI=((retirement home*))</li> </ol>
	Subject Headings
	<ol> <li>Exp diet supplementation/ OR eating/ OR food intake/ OR diet therapy/ OR food analysis/</li> </ol>
	2. Exp home for the aged/ OR exp residential home/ OR exp nursing home/ OR exp nursing home patient/
	Note:
	<ul> <li>EXP Food supplementation         <ul> <li>(used for: diet additive, diet supplement, dietary supplement, dietary supplementation dietary supplements, food supplement; food, fortified; nutritional supplementation, supplementary diet)</li> <li>(EXP includes: )</li> </ul> </li> </ul>
	<ul> <li>Diet therapy         <ul> <li>(used for: diet treatment, dietary therapy, dietary treatment, nutrition therapy)</li> </ul> </li> </ul>
	<ul> <li>EXP nursing home         <ul> <li>(used for: convalescence home, nursing homes, skilled nursing facilities)</li> </ul> </li> </ul>
	<ul> <li>EXP Nursing home patient         <ul> <li>(used for: long term care patient, nursing home resident)</li> </ul> </li> </ul>
	<ul> <li>EXP Home for the aged         <ul> <li>(used for: homes for the aged, housing for the elderly, old age home, old people home)</li> </ul> </li> </ul>
	<ul> <li>EXP residential home         <ul> <li>(used for: group home, residential facilities, residential institution)</li> </ul> </li> </ul>
	<ul> <li>DID NOT USE Long term care here, because:         <ul> <li>(Used for: chronic treatment, life support care, long term therapy, long term treatment; medical care, long term; treatment, long</li> </ul> </li> </ul>
EMBASE	term)
	<ul> <li>Author Key words</li> <li>1. (Fortified adj2 food\$).tw. OR (food fortif\$).tw. OR eating.tw. OR (food\$ adj2 intake\$).tw. OR (oral\$ adj2 intake\$).tw. OR ((food\$ or meal\$ or drink\$ or beverage\$ or diet\$ or snack\$ or breakfast\$ or break-fast\$ or lunch\$ or dinner\$) adj5 (fortif\$ or enrich\$ or supplement\$)).tw. OR (food\$ adj2 enhance\$).tw.</li> </ul>
EMBASE	<ol> <li>(long term care\$ or long-term care\$ or nursing home\$ or retirement home\$ or residential facilit\$).tw. OR (geriatric adj2 (home\$ or unit\$ or facilit\$ or institution\$)).tw.</li> </ol>

Authors Length No. of Mean Age Unique <50% RDA\* 50-99% RDA\* >99% RDA\* participa (Unless stated Characteristics [Total or Male/Female, unless [Total or Male/Female, unless [Total or Male/Female, unless otherwise) and Notes stated otherwise] stated otherwise] stated otherwise] nts Weighed Food Records (WFR) Wendland et 21 -day Cognitively Ca (458±140 mg) C (75.6±28.7 mg) A (1180±700 µg RE) 23 86(6)y al., 2003 WFR (M=3, impaired residents B1 (0.7±0.2 mg) Fe (12.3±3.7 mg) who retained the (Canada) F=20) B2 (1.2±0.4 mg)  $P(789\pm 228 \text{ mg})$ ability to feed B3 (9.0±2.9 NE) themselves Garcia-Arias 124 80.5(6.5)v Nursing home Folate (211.9±47.0/202.5±44.7 C (119.2±53.5/118.6±35.7 mg) 7-dav et al., 2003 WFR (M=60, (range: 65-98y) residents B12  $(2.7 \pm 1.4/3.0 \pm 0.7 \mu g)$ μg) F=64) (Spain) Fe  $(17.0\pm7.4 \text{ mg}/11.8\pm1.5 \text{ mg})$ Moreiras-7-day 53 82y (range: 68-Healthy, A (329±54/310±62 µg) B1  $(0.9\pm0.08/0.9\pm0.09 \text{ mg})$ C (123±10/113±21 mg) Varela et al., WFR 91y) institutionalized D (0.7±0.2/0.6±0.3 µg) B2 (0.9±0.07/0.9±0.13 mg) B3  $(24\pm 2/22\pm 2 \text{ mg})$ (M=19, B12  $(4\pm 1/4\pm 1 \mu g)$ 1986 (Spain) W=34) adults Folate  $(139 \pm 18/131 \pm 23 \mu g)$ Mg  $(223\pm17/204\pm20 \text{ mg})$  $Ca (394 \pm 79/380 \pm 100 \text{ mg})$  $Zn (9\pm 1 \text{ mg} - \text{male})$ Fe  $(11\pm 1/10\pm 1 \text{ mg})$ I (162±59/151±70 µg)  $Zn (9 \pm 1mg - female)$ 52 84(7.3)v Multimorbid D (3.9 ug) A (1157 ug RE) B2 (1.4 mg) Lammes et 5-day al., 2009 WFR (M=11, M=81(7.8)y, residents: E(4.6 mg)C (61 mg) B3 (19 NE) (Sweden) F=41) F=85(6.9)y WFR repeated 3x Folate (168 µg) B1 (0.95 mg) B12 (6.3 µg) over 1.5 years Mg (203 mg) B6 (1.2 mg) P (975 mg) K\* (2122 mg) Ca (824 mg) Na (2246 mg) Se (25 µg) Fe (6.7 mg) Zn (7.1 mg) 52 84(7.3)y Multimorbid D (4.5±1.4/3.5±1.3 µg)  $C (48\pm 26 \text{ mg} - \text{female})$ A (1845±856/1341±1000 µg Lammes et 5-dav al., 2006 WFR (M=11, M = 81(7.8)y, residents: E (4.8±1.2/4.2±1.4 TE) B1  $(1.1\pm0.3/0.9\pm0.3 \text{ mg})$ RE) (Sweden) F=41) WFR repeated 3x C (41±17 mg - male) B6  $(1.4\pm0.3/1.2\pm0.3 \text{ mg})$ F=85(6.9)y B2  $(1.4\pm0.4/1.4\pm0.5 \text{ mg})$ Folate (168±50/162±60 ug) over 1.5 years Ca  $(791\pm 264/812\pm 275 \text{ mg})$ B3 (24±5/19±5 NE)  $K^* (2280 \pm 422/2130 \pm 543 \text{ mg})$ Fe  $(7\pm 1/6\pm 2 \text{ mg})$  $B12 (8 \pm 6/8 \pm 7 \text{ µg})$ Mg  $(220\pm 40/202\pm 51 \text{ mg})$  $P(1054\pm 267/974\pm 26 \text{ mg})$ Se  $(26\pm 8/25\pm 7 \mu g)$  $Zn(8\pm 2/7\pm 2 mg)$ Na (2794±707/2197±459 mg) Barr et al.. 5-day 30 90.6y Female LTC Ca (518.4±210.4 mg) A (635±254 µg RE) C (76.9±34.8 mg) 1984 WFR (range: 81residents B1  $(0.74 \pm 0.20 \text{ mg})$ B3 (15.8±4.6 mg NE) [Canada] 102y)  $B2 (1.02 \pm 0.37 \text{ mg})$ Fe (8.1±1.8 mg)  $Zn (6.0 \pm 1.7 \text{ mg})$ Perez-Llama 86 (M=29. Residents from 3 D (3.90±4.64/2.49±1.15 µg) Ca (851±211/838±259 mg) 4-dav 77.4(8.1)y et al., 2008 F=57) M=72.2(7.0)y, nursing homes; WFR F=80.4(7.2)y WFR included food (Spain) and fluids at meals 252 Folate (220±79 µg - male) 78.9(7.6)y Nursing home Folate (199±76 µg - female)  $C(166 \pm 71/153 \pm 69 \text{ mg})$ Lopez-4-day Contreras et WFR (M=101, M=76.1(8.0)y, residents B12  $(4.37 \pm 2.98/3.88 \pm 2.06 \mu g)$ al., 2010 F=151) F=80.7(6.8)y Fe  $(13.6 \pm 4.4/11.5 \pm 3.5 \text{ mg})$ (Spain)

**Table 2.** Micronutrients of Concern from Intake Studies (by type and length of study)

Vir et al., 1979 (Ireland)	3-day WFR	26 (M=9, F=17)	80.6y (range 65-95y)	Residential accommodation; EFR filled by the caretakers	D (1.25±0.68/1.07±0.39 µg) C (36.7±13.07/31.1±9.53 mg)	B1 (0.83±0.18/0.81±0.14 mg) B6 (1.17±0.39/0.93±0.18 mg) Ca (892±81.8/868±142.7 mg) Mg* (224±39/185±28 mg) K* (2285±491/2094±363 mg)	A (790±185.7/972±449.6 μg) B2 (1.42±0.33)/1.30±0.39 mg) Fe (9.5±2.58/8.2±1.71 mg)
Deijen et al., 2003 (The Netherlands)	3-day WFR + EFR	90 (M=12, F=78)	M= 79.5y, F=83.7y	Elderly psycho- geriatric nursing home residents		C (53mg) B3 (8.27 mg) B6 (0.92 mg)	
Lengyel et al., 2008 (Canada)	3-day WFR + EFR 3-day	48 (M=17, F=31)	88(8)y M=86(9)y, F=89(7)y 69-94y	LTC residents on regular diet; WFR included meals only), EFR included meals and snacks, *Weighed values are in medians, † E(mg aT = total E x 0.8) Residents	<b>Observation method:</b> D (5.7±2.3/4.4±2.2 μg, >70y) E (6.4±2.3 mg aT - female) Folate (196±59/161±78 μg) <b>Weighed method:</b> Folate (149±68 μg) Mg (170±58 mg)	Observation method:           C ( $78\pm45 \text{ mg} - \text{male}$ )           E ( $10.2\pm4.2 \text{ mg} \text{ aT} - \text{male}$ )           B1 ( $1.0\pm0.2 \text{ mg} - \text{female}$ )           B6 ( $1.4\pm0.5/1.1\pm0.3 \text{ mg}$ )           Ca ( $783\pm268/600\pm261 \text{ mg}$ )           Mg ( $232\pm73/175\pm38 \text{ mg}$ )           Zn ( $7.5\pm2.3/5.6\pm2.3 \text{ mg}$ )           Weighed method:           C ( $57\pm28 \text{ mg}$ )           E ( $7.9\pm4.1 \text{ mg} \text{ aT}$ )           B1 ( $1.0\pm0.3 \text{ mg}$ )           B6 ( $1.1\pm0.4 \text{ mg}$ )           Zn ( $5.6\pm2.5 \text{ mg}$ )           B1 ( $1.0\pm0.4 \text{ - female mg}$ )	Observation method:A (1770 $\pm$ 774/1163 $\pm$ 693 µg)C (76 $\pm$ 48 mg - female)B1 (1.3 $\pm$ 0.4 mg - male)B2 (1.8 $\pm$ 0.4/1.4 $\pm$ 0.4 mg)B3 (24.7 $\pm$ 5.8/18.9 $\pm$ 4.2 NE)B12 (7.2 $\pm$ 5.3/4.7 $\pm$ 4.2 µg)Fe (12.2 $\pm$ 3.3/9.4 $\pm$ 2.7 mg)Weighed method:(Weighed intake of A, D, andB3 not provided)B2 (1.4 $\pm$ 0.5 mg)B12 (3 $\pm$ 4.7 µg)Fe (9.3 $\pm$ 3.1 mg)A (929 $\pm$ 203/726 $\pm$ 185 µg RE)
al., 1997 (Australia)	WFR	(M=6, F=13)		consuming a normal diet		Ca (812±309/638±203 mg) Fe (6.6±1.7 mg - female) Mg (234±57.3/161±41.3 mg) Zn (7±3/5.6±1.3 mg)	C (110±37/95±49 mg) B1 (1.4±0.3 mg - male) B2 (1.8±0.6/1.4±0.5 mg) B3 (26.7±5.0/19.5±4.5 mg NE) Fe (8.7±1.7 mg - male) P (1345±404/971±234 mg)
Sturtzel et al., 2010 (Austria)	3-day WFR	30	86.0(9.0)y (Fiber intervention group), 84.6(11.4)y (Control group)	Frail patients with multiple chronic diseases; inclusion criteria: oral intake with laxative use as a therapy; baseline total values used here	B6 (0.73±0.52 mg) Folate (105.3±42.9 μg)	B12 (1.9±1.3 μg)	
Germain et al., 2006 (Canada)	2-day WFR	9 (M=4, F=5)	84.6(3.81)y	Residents with BMI <24 or >7.5% weight loss within past 3 months, with dysphagia	D (4.45±1.81 μg)	Ca (757±209 mg) Mg (256±50.8 mg) K* (2885±625 mg) Zn (8.88±3.50 mg)	C (155±51.4 mg) B1 (1.63±0.74 mg) B2 (1.93±0.97 mg) B3 (22.3±6.54 NE) B12 (2.57±1.39 µg) Fe (13.5±4.97 mg) P (1107±251 mg) Na (2519±624 mg)

Lowik et al., 1992 (The Netherlands)	1-day WFR + 9- day EFR	54	83(8)y	Elderly women living in a nursing home; EFR done	B6 (0.82±0.24 mg)	A (670±180 µg RE) B1 (0.65±0.18 mg) Ca (910±430 mg) Fe (7.6±2.3 mg) K* (2340±660 mg)	C (54±27 mg) B2 (1.37±0.54 mg) P (1090±420 mg)
Sempos et al., 1982 (US)	1-day WFR (all meals)	162, 12 per home (M=54, F=108)	M= 80y, range: 28-101y F = 80y, range: 23-101y	Residents from 14 nursing homes	Mg: (209±55 mg - male)	C $(81\pm69/72\pm58 \text{ mg})$ B1 $(1.08\pm0.39/0.89\pm0.30 \text{ mg})$ B3 $(12.5\pm5.5/10\pm4.7 \text{ mg})$ B5* $(4.85\pm2.36/4.06\pm2.25 \text{ mg})$ B6 $(1.14\pm0.35/0.98\pm0.04 \text{ mg})$ Folate (Folic acid) $(240\pm83/213\pm94 \mu \text{g})$ Ca $(828\pm256/677\pm291 \text{ mg})$ Mg $(168\pm55.0 \text{ mg} - \text{female})$ Zn $(9.6\pm3.6/7.8\pm3.0 \text{ mg})$	A (7924±14289)/7865±12793 IU) B2 (1.96±1.11/1.58±1.08 mg) B12 (8.9±21.2/7.4±8.8 μg) Fe (12.21±4.52/9.12±3.56 mg)
Estimated Fo	od Records (	EFR)					
Johnson et al., 1995 (US)	7-day EFR	51, Regular diet: 31, Pureed diet: 20	85y (both groups)	Female nursing home residents; (Regular and pureed consistency meals with Consumption Monitoring System (observation from returned trays))	Meals, snacks, nutrient supplements [Regular/Pureed] D (3.90±1.93/3.28±1.28 μg) Folate (189±62/166±22 μg)	E (13.0±3.8/12.0±2.4 mg) C (89.0±29.0 mg - male; regular) B1 (1.0±0.2 mg; pureed) B6 (1.4±0.5/1.1±0.3 mg) Ca (660±243/667±170 mg) K* (2116±492/2148±322 mg) Zn (6.8±2.0/6.1±1.3 mg; pureed)	B1 (1.2±0.3 mg; regular) B2 (1.5±0.4/1.4±0.2 mg) B12 (3.6±1.3/3.2±0.8 μg) C (104.0±18.0 mg; pureed) Fe (10.0±3.0/8.0±1.0 mg)
Beck et al., 2002 (Denmark)	4-day EFR	104	80-85y (range)	Nursing home residents	Multiplied nutrient intake by MJ [<10E% sugar/10-20E% sugar/ ≥20E% sugar] D (2.41/2.46/1.72 μg) E (3.56/3.45/2.58 mg): B1 (0.59 mg; >20%E) B6 (0.73 mg; >20%E) Folate (197.1/207.9/151.8 μg) I (71.6/62.7 μg; 10-20%E/ >20%E)	A (686.4 RE; >20% E) C (49.6/55.4/38.9 mg) B1 (0.80/0.77 mg; <10% E/10- 20% E) B2 (1.25 mg; >20% E - male) B6 (1.02/1.00 mg; <10% E, 10- 20% E) Ca (1080.4/1070.3/838.2 mg; <10% E/10-20% E/>20% E), I (97.1 $\mu$ g; <10% E) Fe (7.59/7.01/5.61 mg; <10% E/10-20% E/>20% E), Zn (6.53 mg; >20% E) Zn (9.27/8.62 mg - male; <10% E/10-20% E)	A (1043.9.1/1078 RE; <10%E/10-20% E) B2 (1.53/1.54 mg; <10%E/10- 20% E) , B12 (4.60/4.47/3.10 μg)

Odowd et al., 1993 (US)	3-day EFR + FFQ	109, Site A: 57, Site B: 52	82(1.0)y (Site A) 81(1.3)y (Site B)	Residents from a private nursing home (site A) or public LTC wing (site B); (Estimated EFR used for cognitively impaired residents by nursing staff (51%), FFQ for cognitively well)	D intake (1.33±1.28 µg; food only)		
Grieger et al., 2007 (Australia)	3-day EFR (plate waste)	169, HLC: 93, LLC: 76	83.3(8.5)y	LTC residents	D (1.78±2.05 µg)§ §Value is the median (inter-quartile range)	Folate (248±114 µg) Ca (796±356 mg) Zn (9.4±0.6 mg - male; 7.7±0.3 mg - female)	
Lee et al., 2002 (Canada)	3-day EFR (plate waste)	53 (M=8, F=45)	M=83(9)y, F=86(7)y	Residents from 3 LTC facilities. Included dietary intake values only.	D (6.35±2.28/4.68±2.18 μg), Ca (560±198 mg- female)	Ca (847±264 mg - male)	
Hall et al., 2010 (Canada)	3-day EFR (meals and snacks)	30 (M=27, F=3)	87.2(4.1)y (range: 80-96y)	Residents in complex continuing care residents in Veterans Centre	D (5.18 μg)		
Gloth et al., 1995 (US)	3-day EFR	64	81(8)y (Combined nursing home and private dwelling)	Sunlight-deprived residents; Inclusion criteria: free of diseases/medication s that interfere with D status, confined indoors for at least 6 months	D (7.05±3.65 µg)	Ca (921±377 mg)	
Aghassi et al., 2007 (Canada)	3-day EFR	407 (M=108, F=299)	85.2(7.7)y M=83.8(7.5)y, F=85.7(7.8)y	LTC residents; Excluded: inability to take tablets, already receiving supplementation	E (6.2±1.9/6.2±2.8 mg) B6 (0.5±0.5 mg - female)	B3 (15.3±4.5mg - male) B6 (1.4±0.4 μg - male) Folate (260.0±82.9/252.2±88.0 μg) Zn (8.5±2.4 mg - male)	[Male/Female] A ( $1122\pm877/1036\pm761 \ \mu g$ ), C ( $109.8\pm49.0/119.1\pm58.1 \ mg$ ) B1 ( $1.3\pm0.4/1.3\pm0.4 \ mg$ ) B2 ( $1.7\pm0.5/1.6\pm0.5 \ mg$ ) B3 ( $14.6\pm4.7 \ mg$ ) B12 ( $4.4\pm4.8/3.9\pm4.3 \ \mu g$ ) Cu* ( $1.1\pm0.5/1.1\pm0.5 \ mg$ ) Fe ( $11.1\pm3.5/10.7\pm3.6 \ mg$ ) Mg ( $654.6\pm228.7/639.0\pm242.9 \ mg$ ) Zn ( $8.2\pm2.7 \ mg$ - female)

Liu et al., 1997 (Canada)	3-day EFR	155 (M=77, F=78)	83.2(7.1)y	LTC residents from 3 facilities without conditions interfering with D metabolism; 24 participants for EFRs (assessed every 4th participant)	D (4.93±2.55 μg)		
Gloth et al., 1996 (US)	3-day EFR	47	78.7(1.3)y	Nursing home resident values only	D (7.05±0.53 μg), Mg (208±16 mg)	B3 (15.5±1.4 mg - male) B6 (1.54±0.15 mg - male) Folate (215±25 μg) Ca (921±55 mg) Zn (8.7±0.8 mg - male)	C (104±11 mg) B1 (1.52±0.12 mg) B2 (2.02±0.13 mg) B12 (4.04±0.37 μg) Fe (11.5±0.8 mg)
Nowson et al., 2003 (Australia)	1-day EFR (plate waste at meals)	139 (M=35, F=104)	83.3(9.8)y	Nursing home residents from 9 sites; Both statuses worsen as diet becomes downgraded	Mean nutrient intake (95% CI): Ca (359(333, 385) mg) D (1.0(0.9,1.0) μg); [Not impaired/impaired eating in Nursing Home] (95% CI): <b>Ca (mg):</b> Overall: 343(286,399)/362(334,362) Full: 406(313,496)/310(242,378) Soft: 286(151,421)/376(327, 425) Pureed: 292(226,358)/382(342,422) <b>D (μg):</b> Overall: 0.9(0.8,1.1)/0.9(0.8,1.0) Full: 1.1(0.9,1.4)/0.8 (0.6,0.9) Soft: 0.7(0.4,1.1)/0.8(0.6,1.0) Pureed: 0.7(0.5,1.0)/1.1(1.0,1.2)		
Webb et al., 1990 (US)	<b>Dietary</b> survey	38, Group A: 21, M=5, F=16 Group B: 17, M=7, F=10	81(8)y (Group A) 82(9)y (Group B)	<b>Group A:</b> moderate supervision of ADLs, partial day outdoors; <b>Group B:</b> 24-h skilled nursing care, from constant supervision to bedridden; Observed EFR (amount delivered vs returned) for milk only; estimated general intake from menus for other foods	Overall maximum daily D intake for the center: < 5 μg; D (Excluding milk: 0.6 μg, estimated average intake), (Including milk: 1.3-8.8 μg, range of maximum intake)		

Other							
Gonzalez et al., 2007 (Spain)	FFQ	227 (M=93, F=134)	M=72.9(7.2)y, F=76.4(5.9)y	Nursing home residents from 14 nursing homes; Home-specific FFQ			Se (100.1±31.6/98.7±23.7 µg)
Lasheras et al., 2003 (Spain)	FFQ	140 (M=59, F=81)	M=73.3(5.6)y, F=74.2(4.8)y	Institutionalised elderly subjects from 7 institutions; FFQ was specific to each home; food grouping to identify sources of B2, Folate, B12	Folate (187.3±81.1 μg)		B2 (1.8±0.5 mg) B12 (4.9±1.8 μg)
Oudshoorn et al., 2012 (The Netherlands)	24-hr dietary recall	426 (M=111, F=315)	81.0(7.2)y	Residential homes residents		Ca (826±242 mg)	
Rumbak et al., 2010 (Canada)	24-hr dietary recall	339 (M=62, F=277)	61-93y (range)	Residents from 11 nursing homes in Zagreb	Ca (599.1±259.9 mg - female)	Ca (607.6±291.1 mg - male)	Fe (9.4±3.4/8.2±3.0 mg)
Van der Wielen et al., 1996 (The Netherlands)	4 wk Diet history	40	81.5(7.1)y	Female nursing home residents	C (56±26 mg)	B1 (0.81±0.18 mg) B2 (1.20±0.36 mg - male) B6 (0.96±0.19 mg)	
Vikstedt et al., 2011 (Finland)	1-day Diet history	375 (M=67, F=308)	83y	Service house residents	D (7.5/6.6 µg) E (6.8/6.0 mg)	Folate (272/220 µg) Ca (1106 mg - female)	C (mg): 104/101, Ca (1247 mg - male)

WFR = Weighed Food Record, EFR = Estimated Food Record;

 $B1 = thiamin, B2 = riboflavin, B3 = niacin, \alpha T = alpha-tocopherol; Ca = calcium, Cu = copper, Fe = iron; M = male, F = female; Wk = week, hr = hour results of the second seco$ 

\*AI used for Copper (Cu), Pantothenic acid (B5), and Potassium (K)

	Table 3. Biochemical Data Compared to Reference Values (AMA, CDC, Paper references)									
Micronutrients Examined/	Names of Authors	Value, (Mean(SD) for total, unless	AMA	CDC		Number of participants				
Method	(Country)	otherwise specified)	[REF]	[REF]	Papers					
Vitamin A	Vir et al., 1979	M:49.7(11.0) µg/dL								
Serum carotene	(Ireland)	F: 91.4(48.2)µg/dL	N	N/A	N	N=26 (M=9, F=17)				
Vitamin D	Gloth et al., 1995	50.7(24.7) pmol/L								
1,25(OH)2D	(US)		L	N/A	N	N=64				
	Odowd et al., 1993	72.3(3.90) pmol/L								
	(US)		N	N/A	N	N=109				
		T: 145(85) pmol/L								
	Perez-Llama et al.,	M: 131(70) pmol/L								
	2008 (Spain)	F: 153(94) pmol/L	N	N/A	N	N=86 (M=29, F=57)				
Vitamin D	Gloth et al., 1995	36.2(17.7) nmol/L	N	T	N	NL CA				
25(OH)D	(US)		N	L	N	N=64				
	Johnson et al., 2008	Octogenarian: 72.1(26.7) nmol/L Centenarian: 70.1(33.3) nmol/L				Octogenarians: N=12				
	(US)	Centenarian: 70.1(55.5) http://L	N	Ν	Ν	Centenarian: N=99				
	Lowik et al., 1992	F: 28(16) nmol/L	N	IN	IN	Centenarian. IN-99				
	(The Netherlands)	Г. 28(10) IIII0I/L	L	L	L	N=51				
	Odowd et al., 1993	6.37(0.32) nmol/L	L		L	N-51				
	(US)	0.37(0.32) 11110/12	L	L	L	N=109				
	Oudshoorn et al.,		L			11-109				
	2012 (The	39.1(21.4) nmol/L				N=426 (M=111,				
	Netherlands)	33.1(21.4) IIII0/E	N	L	Ν	F=315)				
	rectionands)	T: 50.1(32.4) nmol/L				1-515)				
	Perez-Llama et al.,	M: 53.4(26.5) nmol/L		N male	N male					
	2008 (Spain)	F: 48.2(35.7) nmol/L	Ν	L female	L female	N=86 (M=29, F=57)				
		Winter:								
		M: 41.9 (13.7) nmol/L								
		F: 35.7(20.2) nmol/L								
		Summer:								
	Sem et al., 1987	M: 39.9(13.5) nmol/L								
	(Norway)	F: 48.4(22.2) nmol/L	N	L	L	N=56 (M=21, F=35)				
		T: 58.5(24.9) nmol/L								
		M: 62.0(16.5) nmol/L								
	Sitter et al., 2011	F: 55.5(31.7) nmol/L								
	(Canada)		N	N	N/A	N=14 (M=5, F=9)				
	Vir et al., 1979	Serum 25(OH)D (no actual values								
	(Ireland )	but paper identified as low)	N/A	N/A	N/A					
	Webb et al., 1990	Range: 27.5 - 37.5 nmol/L				N. 20				
	(US)	(Used mid-range value as cut-off)	L		L	N=38				
	Woods et al., 2009	M: 51.5(46.8) nmol/L	N	N male	N male	N 105 (M 02 E 70)				
Vitamin E	(Australia) Lowik et al., 1992	F: 38.0(41.0) nmol/L F: 28.0(9.5) μmol/L	N	L female	L female	N=105 (M=23, F=72)				
Alpha-tocopherol	(The Netherlands)	F: 28.0(9.5) μmol/L	N/A	N/A	Ν	N=51				
Vitamin C	Lowik et al., 1993	F: 37.8(19.4) µmol/L	IN/A	IN/A	IN	N-31				
Cell ascorbic acid	(The Netherlands)	Γ. 57.8(19.4) μΠΟΙ/L	N/A	N/A	N/A	N=54				
Vitamin C	(The rechending)		11/71	11/1	11/1	11-J4				
Leukocyte	McClean et al.,	M: 11.1(5.5) ug/10 <sup>8</sup> WBC								
ascorbic acid	1977 (New Zealand)	111. 11.1( <i>J.J.</i> ) ug/10 WDC	N/A	N/A	Ν	N=35				
Vitamin C			11/11	11/11	11	11-55				
Plasma ascorbic	Lowik et al., 1992	F: 35.0(20.1) μmol/L								
acid	(The Netherlands)		Ν	Ν	Ν	N=51				
	Lowik et al., 1993	F: 23.7(18.4) µmol/L								
	(The Netherlands)		Ν	Ν	Ν	N=54				
	(			L Eden						
				(L to						
		Edentulous (Eden): 11.4 µmol/L*		borderline		Dentate, n=57				
	Marcenes et al.,	Dentate (Den): 31.0 µmol/L*	L Eden	deficient)		Edentulous, n=139				
	2003 (UK)	*Median	N Den	N Den	N/A					
	McClean et al.,	M: 16(15) μmol/L								
	1977 (New Zealand)		L	L	L	N=35				

**Table 3.** Biochemical Data Compared to Reference Values (AMA, CDC, Paper references)

		M: 9.65(7.95) µmol/L		L male		
	Vir et al., 1979	F: 23.3(12.5) μmol/L	L male	(deficient)	L male	
	(Ireland)	N 100(0.07)	N female	N female	Nfemale	N=26 (M=9, F=17)
Thiamin	Vir et al., 1979	M: 1.09(0.07) F: 1.09(0.09)				
ETK - EC 2.2.1.1	(Ireland)	1. 1.09(0.09)	N/A	N/A	N	N=26 (M=9, F=17)
Riboflavin	(included)	M: 1.03(0.07) mg/dL	11/71	14/14	1	14-20 (14-2, 1-17)
EGR AC - EC	Vir et al., 1979	F: 1.03(0.11) mg/dL				
1.6.4.2	(Ireland)	1.1.05(0.11) mg/d2	N/A	N/A	Ν	N=26 (M=9, F=17)
Vitamin B6	(	M: 1.20(0.11) mg/dL				
EGPT index - EC	Vir et al., 1979	F: 1.23(0.18) mg/dL				
2.6.1.2	(Ireland)		N/A	N/A	Ν	N=26 (M=9, F=17)
Vitamin B6						
Pyridoxal 5'	Lowik et al., 1992	F: 31(39) nmol/L				
Phosphate	(The Netherlands)		N	N/A	Ν	N=51
Vitamin B6		M: 23.9(21.4) nmol/L				
Plasma vitamin	Sturtzel et al., 2010	F: 21.4(21.4) nmol/L				
B6	(Austria)		N	N/A	N	N=30
Folate	Lowik et al., 1992	F: 3.13(1.54) ng/mL				
Plasma folate	(The Netherlands)		N	N	L	N=51
	Sturtzel et al., 2010	M: 2.16(1.12) ng/mL	-			N. 20
	(Austria)	F: 2.34(1.21) ng/mL	L	N	L	N=30
Folate	Huerta et al., 2004	6.31(4.10) ng/mL	N	NT	NT/A	N 140 (M 50 E 01)
Serum folate	(Spain) Vir et al., 1979	$M_{1,2} = 2(1, 42) = -4\pi I$	N	N	N/A	N=140 (M=59, F=81)
	(Ireland)	M: $3.8(1.42)$ ng/mL	Ν	Ν	Ν	N = 26 (M = 0 E = 17)
Vitamin B12	(Ireland)	F: 6.7(4.44) ng/mL	IN	IN	IN	N=26 (M=9, F=17)
Plasma Vitamin	Lowik et al., 1992	F: 748(1367) pg/mL				
B12	(The Netherlands)	r. 748(1507) pg/mL	Ν	N/A	N	N=51
D12	Sturtzel et al., 2010	M: 385.7(217.6) pg/mL	1	IN/A	1	N=51
	(Austria)	F: 468.6(593.7) pg/mL	Ν	N/A	Ν	N=30
Vitamin B12	(Plustilu)	1.400.0(000.0) pg m2	14	1.0/21	11	11-50
Serum vitamin	Huerta et al., 2004	395(218) pg/mL				
B12	(Spain)	···· (·) F8	Ν	N/A	N/A	N=140 (M=59, F=81)
		With MV:				
		M: 337(134) pg/mL				
		F: 396(198)pg/mL				
		Without MV:				
	Mirkazemi et al.,	M: 321(121) pg/mL				
	2012 (Australia)	F: 381(188) pg/mL	N	N/A	N	N=130
	Vir et al., 1979	M: 276.7(156.9) pg/mL				
	(Ireland)	F: 351.5(150.9) pg/mL	N	N/A	Ν	N=26 (M=9, F=17)
Calcium	GL 1 1 1005	1.00(0.10) 1/7				
Ionized serum	Gloth et al., 1995	1.28(0.12) mmol/L		27/4		
calcium	(US)	2 295 (0.01)	N	N/A	N	N=64
Calcium Serum calcium	Odowd et al., 1993	2.385 (0.01) mmol/L	N	NI/A	NI/A	N 100
Serum calcium	(US)	T: 2 20(0 12) mm = 1/I	N	N/A	N/A	N=109
	Perez-Llama et al.,	T: 2.39(0.12) nmol/L M: 2.42(0.08) nmol/L				
	2008 (Spain)	F: 2.37(0.13) nmol/L	Ν	N/A	N	N=86 (M=29, F=57)
	2000 (Spain)	M: 2.39(0.12) mmol/L	1N	11/21	11	11-00 (11-27, F=3/)
		F: 2.36(0.15) mmol/L				
	Sem et al., 1987	*Using without supplement				
	(Norway)	values	Ν	N/A	Ν	N=56 (M=21, F=35)
	Vir et al., 1979	T: 2.3(0.11) mmol/L				× 77
	(Ireland)	F: 2.4(0.14) mmol/L	Ν	N/A	N	N=26 (M=9, F=17)
	Webb et al., 1990	2.40(0.13) mmol/L			- 1	
	(US)		Ν	N/A	N/A	N=38
					N male	
		M: 2.17(0.12) mmol/L			L female	
	Worwag et al., 1999	F: 2.14(0.10) mmol/L			(Low	N=117 (M=20, F=97*)
	(Germany)		N	N/A	normal)	*97F for Ca, K, Na
Calcium	Gloth et al., 1995	11.9(7.5) ng/mL				
Osteocalcin	(US)		Ν	N/A	Ν	N=64
	•	•		*		<u>.</u>

		T: 102.4(3.3) mmol/L				
	Sitter et al., 2011	M: 101.8(2.9) mmol/L				
Chloride	(Canada)	F: 102.8(3.7) mmol/L	Ν	N/A	N/A	N=14 (M=5, F=9)
	· · · ·		IN	IN/A	IN/A	
Copper Serum copper	Bonaccorsi et al.,	F: 1268.30(249.35)µg/L	Ν	N/A	Ν	N=428 (M=101, F=327)
Serum copper	2013 (Italy)	T: 85.2(25.2) ng/mL	IN	IN/A	IN	F=327)
Iron	Garcia-Arias et al.,	M: 94.4(27.9) ng/mL				
Ferritin	2003 (Spain)	F: 64.3(20.2) ng/mL	Ν	N/A	N/A	N=124 (M=60, F=64)
rennun	2003 (Spain)	T: 43.7(6.3)%	IN	IN/A	IN/A	IN-124 (IN1-00, F=04)
Iron	Garcia-Arias et al.,	M: 43.8(5.4)%				
Hematocrit	2003 (Spain)		Ν	N/A	N/A	N = 124 (M = 60 E = 64)
Hematocht	Lowik et al., 1992	F: 43.8(6.7) % F: 42.6(4.3)%	IN	IN/A	IN/A	N=124 (M=60, F=64)
	(The Netherlands)	Г: 42.0(4.5)%	Ν	N/A	N/A	N=51
	(The Neulenanus)	T:14.3(1.3) g/dL	19	IN/A	IN/A	11-51
Iron	Garcia-Arias et al.,	M: 14.8(1.3) g/dL				
	,		Ν	N/A	N/A	N = 124 (M = 60 E = 64)
Hemoglobin	2003 (Spain)	F: 14.0(1.2) g/dL	IN	IN/A	IN/A	N=124 (M=60, F=64)
	Lowik et al., 1992	E. 12 $4(1.45) \approx 41$	L	N/A	Ν	N=51
	(The Netherlands) Vir et al., 1979	F: 13.4(1.45) g/dL M: 13.9(2.00) g/dL	L male	IN/A	IN	IN=31
	(Ireland)	F: 14.3(1.70) g/dL	N female	N/A	Ν	N=26 (M=9, F=17)
	Woods et al., 2009	M: 13.2(1.8) g/dL	IN IEIIIaie	IN/A	1	IN-20 (INI-9, I'-17)
	(Australia)	F: 12.7(1.2) g/dL	L	N/A	Ν	N=105 (M=23, F=72)
	(Australia)	T: 85.2(25.2) μg/dL	L	IN/A	IN	11-103 (11-23, F-72)
Iron	Garcia-Arias et al.,	M: 93.8(40.7) μg/dL				
Serum Iron	2003 (Spain)		Ν	N/A	N/A	N = 124 (M = 60 E = 64)
Serum non	2005 (Spain)	F: 82.0(28.4) μg/dL	IN	IN/A	IN/A	N=124 (M=60, F=64)
	Sitter et el 2011	T: 68.2(29.1) μg/dL M: 68.2(23.5) μg/dL				
	Sitter et al., 2011		Ν	N/A	N/A	N = 14 (M = 5 E = 0)
	(Canada)	F: 68.2(33.5) µg/dL	IN	IN/A	IN/A	N=14 (M=5, F=9)
	Vir et al., 1979	M: 92.8(24.1) $\mu$ g/dL	Ν	N/A	N/A	N = 26 (M = 0 E = 17)
Inon	(Ireland ) Vir et al., 1979	F: 104.2(48.6) µg/dL	IN	IN/A	IN/A	N=26 (M=9, F=17)
Iron	,	M: 376.7(82.3) μg/dL	N	NI/A	NT/A	$\mathbf{N} \rightarrow (\mathbf{M} + 0 + 17)$
TIBC, fasting	(Ireland)	F: 384.7(48.9) μg/dL	N	N/A	N/A	N=26 (M=9, F=17)
T	D 1	M: 225.7(45.4) mg/dl				N 400 04 101
Iron	Bonaccorsi et al.,	F: 231.6(50.3) mg/dl	N		N	N=428 (M=101,
Transferrin	2013 (Italy)	0.99(0.10) 1/I	N	N/A	N	F=327)
Magnesium	Dave et al., 1987	0.88(0.10) mmol/L	N	NI/A	N	$N_{-75}$ ( $M_{-72}$ E-2)
Serum	(US)	M 0 70(0 07) 1/I	N	N/A	N	N=75 (M=73, F=2)
	Worwag et al., 1999	M: 0.79(0.07) mmol/L	N		N	N 110 (M 20 E 00)
DI 1	(Germany)	F: 0.79(0.09) mmol/L	N	N/A	N	N=119 (M=20, F=99)
Phosphorus Serum	Odowd et al., 1993	1.09(0.016) mmol/L	N	NI/A	NT/A	N. 100
Serum	(US)	1.00(0.10) 1/1	N	N/A	N/A	N=109
	Webb et al., 1990 (US)	1.06(0.16) mmol/L	Ν	N/A	N/A	N=38
Potassium	Worwag et al., 1999	4.39(0.74)/4.23(0.51) mmol/L	IN	IN/A	IN/A	N=117 (M=20, F=97*)
Serum	(Germany)	4.39(0.74)/4.23(0.31) IIIII01/L	Ν	N/A	Ν	N=117 (M=20, F=97*) *97F for Ca, K, Na
Selenium		M: 97.88(50.76) µg/L	IN	IN/A	IN	
	Bonaccorsi et al.,		Ν	N/A	N	N=428 (M=101,
Serum	2013 (Italy)	F: 93.77(43.19) μg/L	IN	IN/A	N	F=327) N=227 ( M=94,
	Gonzalez et al.,	M: 86.7(17.0) $\mu$ g/L	N	NI/A	NI/A	
Salanium	2007 (Spain) Lowik et al., 1992	F: 88.2(16.6) $\mu$ g/L F: 106(18) $\mu$ g/g	N	N/A	N/A	F=134)
Selenium Erythrocyte	(The Netherlands)	F: 106(18) ng/g	N/A	N/A	Ν	N=51
Selenium	Lowik et al., 1992	F: 69(14) ng/g	1N/A	IN/A	1N	11-J1
Plasma	(The Netherlands)	1°. 09(14) IIg/g	Ν	N/A	N	N=51
		M. 127 1(20.2) 1/1	IN	IN/A	N	
Sodium	Worwag et al., 1999	M: 137.1(39.3) mmol/L	N	NT/A	N	N=117 (M=20, F=97*)
Serum	(Germany)	F: 138.8(39.3) mmol/L	N	N/A	N	*97F for Ca, K, Na
Zinc	Bonaccorsi et al.,	M: 13.0(2.29) μmol/L				N=428 (M=101,
Serum	2013 (Italy)	F: 12.5(2.13) μmol/L	N	N/A	Ν	F=327)
	Worwag et al., 1999	M: 13.3(2.0) µmol/L	_			
	(Germany)	F: 13.9(2.9) µmol/L	Ν	N/A	N	N=119 (M=20, F=99)

Micronutrients identified as inadequate by one or more reference(s) are highlighted in grey. T (Total), M (Male), F (Female); N (within normal range), L (low), N/A (not applicable)

N	T	1 0	ew Observational Studies: Ref					
Micronutrients	Metabolite	Substrate	Reference Ranges					
Examined	Measured	used	1) AMA (normal ranges)	(1				
			<ul><li>2) CDC, 2011 (low ranges, unless otherwise specified)</li><li>3) Original paper (low ranges, unless otherwise specified)</li></ul>					
Vitamin A	Carotene	Serum	1) 10-85 μg/dL	3) Vir 1979				
vitamin A	Carotene	Serum	0.2-1.6 μmol/L	3) Vir 1979 4.0 ug/dl				
Vitamin D	1,25(OH)2D	Serum	1) 60-108 pmol/L	3) Gloth 1995				
v Italiilii D	1,25(011)2D	Serum	25-45 pg/mL	36-143pmol/L (normal)				
			25-45 pg/mL	14-55 pg/mL				
				14-55 pg/mL				
				Odowd 1993				
				47-169 pmol/L (normal)				
				18-65 pg/ml				
				Webb 1990				
				Normal: 38- 156 pmol/L (normal)				
Vitamin D	25(OH)D	Serum	1) (plasma)	3) Gloth 1995				
v Italiiii D	23(OH)D	Serum	35-150 nmol/L	25-137 nmol/L (normal)				
			(14-60 ng/mL)	10-55 ng/mL				
			(14-00 lig/lilL)	10-35 lig/lilL				
			2) Deficiency: <30 nmol/L(12	Johnson 2008				
			ng/mL)	Deficiency: < 25 nmol/L				
			Inadequacy: 30-49 nmol/L(12-19	Insufficiency: < 50 nmol/L				
			ng/ml)	Optimal: $\geq 80 \text{ nmol/L}$				
			Sufficient: 50-75 nmol/L(20-30	-				
			ng/mL)	Lowik 1992				
				<31 nmol/L				
				Odowd 1993				
				10-162 nmol/L (normal)				
				4-65 ng/ml				
				Oudshoorn 2012				
				Low: <25 nmol/L				
				Normal:				
				The Netherlands $\geq$ 50 nmol/l				
				United States $\geq$ 75 nmol/l				
				Dames I James 2008				
				Perez-Llama 2008 Deficiency: <25 nmol/L				
				Insufficiency: <50 nmol/L				
				insumenency. < 50 millor/L				
				Sem 1987				
				<50 nmol/L				
				<20ng/mL				
				Vir 1979				
				<9.5 nmol/L				
				<3.8 ng/ml				
				Webb 1990				
				Deficiency: <25 nmol/L				
				Low normal: 37.5 nmol/L				
				(Normal per assay for young				
				adults: 20.0-137.5 nmol/L				
				Woods 2009				
				Deficient: <25 nmol/L				
				Insufficient: 25- 50 nmol/L				
Vitamin E	Alpha-	Serum	1) 5.5-17 µg/mL*	3) Lowik 1992				
	tocopherol		*Medscape reference value used	<12 umol/L				
			(No AMA value)					
			(					
			2) Deficiency <500 µg/dL					

**Table 4.** Scoping Review Observational Studies: Reference Range

Vitamin C	Ascorbic acid	Leukocyte		3) McClean 1977
			1) 22 07 17	<10 ug/10 <sup>8</sup> WBC
Vitamin C	Ascorbic acid	Serum	1) 23-85 μmol/L 0.4-1.5 mg/dL	3) Lowik 1993 (Plasma) Deficient <11 umol/L
			2) Deficient: <11.4 μmol/L Low: 11.4-23 μmol/L	Low: 11-23 umol/L
				McClean 1977 (Plasma)
				Low: <23 umol/L
				Deficient: <12 umol/L
				Vir 1979
				<17 umol/L <0.3 mg/dl
Thiamin	ETK - EC			3) Vir, 1979
Riboflavin	2.2.1.1 EGR AC -			>1.2 3) Vir, 1979
	EC 1.6.4.2			$\geq$ 1.2
Vitamin B6	EGPT index - EC 2.6.1.2			3) Vir, 1979 >1.15
Vitamin B6		Dlasme	1) 20, 121 pmol//	>1.15 3) Lowik 1992
v itamin Bo	Pyridoxine	Plasma	1) 20-121 nmol/L 5-30 ng/mL	3) Lowik 1992 <19 nmol/L
				Sturtzel 2010 (normal)
				>28 nmol/L
Folate	Folate	Serum/Plasma	1) 7-36 nmol/L	>6.8 ng/ml 3) Lowik 1992
			3-16 ng/mL	<5 nmol/L
			2) Low	Sturtzel 2010
			<5 nmol/L <2 ng/ml	>5.9 ug/L (normal)
			<2 lig/lill	Vir 1979
				<8 nmol/L
Vitamin B12	Vitamin B12	C - man	1) 119 701	<pre>&lt;3.5 ng/ml 3) Lowik 1992</pre>
vitamin B12	vitamin B12	Serum	1) 118-701 pmol/L 160-950 pg/mL	<138 pmol/L
			2) Low:	Mirkazemi 2012
			<148 pmol/L	Deficient: 150 pmol/L
			< 200 pg/mL	Borderline/equivocal: 150-250
				pmol/L
				Sturtzel 2010 >200 ng/L (normal)
				Vir 1979
				<111 pmol/L
0.1.1			1) 1 15 1 05 1 15	<150 pg/ml
Calcium	Calcium, Ionized	Serum	1) 1.15-1.27 mmol/L 4.60-5.08 mg/dl	3) Gloth 1995 1.15-1.35 mmol/L (normal)
	IONIZCU			4.61-5.41 mg/dL
Calcium	Calcium,	Serum	1) 2.05-2.55 mmol/L	3) Dave 1987
	Total		(8.2-10.2 mg/dL)	2.13-2.63 mmol/L(normal) 8.5-10.5 mg/dl
				Worwag 1999
Calcium	Osteocalcin	Serum	1) 3.0-13.0 μg/L	2.16-2.60 mmol/L(normal) 3) Gloth 1995
201010111	Concordioni		(3.0-13.0  mg/mL)	2-18 ug/L (normal)
				2-18ng/ml
				Sem 1987 <2.20 mmol/L
				Vir 1979 <8.7mg/dl

Chloride	Chloride	Serum,	1) 96 - 106 mmol/L	
		plasma	(96-106 mEq/L)	
Copper	Serum copper	Serum	1) 11- 22 μmol/L 70 - 140 μg/dL	3) Bonaccorsi 2013 7.9-20 umol/L (normal) 50–125 ug/dL
Iron	Ferritin	Serum	1) 34-450 pmol/L 15-200 ng/ml	
			2) <34 pmol/L (low) < 15ng/mL	
Iron	Hematocrit	Whole blood	1) 0.41-0.50 (proportion of 1.0) 41-50%	3) Woods 2009 Normal M: 0.38-0.54 L/L (normal) F: 0.34 - 0.47 L/L
Iron	Hemoglobin	Whole blood	1) 140-175 g/L (14.0-17.5 g/dL)	3) Vir 1979 Male: <130 g/L Female: <120 g/L
				Woods 2009 Normal M: 125-175 g/L F: 110-160 g/L
Iron	Serum iron	Serum	1) 10.7-26.9 μmol/L (60-150 μg/dL)	
Iron	TIBC, fasting	Serum	1) 44.8-80.6 μmol/L (250-450 μg/dL)	
Iron	Transferrin	Serum	1) 2.5-5.0 μmol/L 200-400 mg/dL	3) Bonaccorsi 2013 27-43 umol/L (normal) 220–350 mg/dl
Magnesium	Magnesium	Serum	1) 0.65-1.05 mmol/L 1.3-2.1 mEq/L	3) Dave 1987 1.8-2.6 mg/dl (normal) Worwag 1999
Phosphorus	Phosphorus	Serum	1) 0.74-1.52 mmol/L 2.3-4.7 mg/dL(tightly regulated,	0.76-1.10 mmol/L (normal) 3) Dave 1987 0.81-1.5 mmol/L(normal)
Potassium	Potassium	Serum	only measure for food intake) 1) 3.5-5.0 mmol/L (3.5-5.0 mEq/L)	2.5-4.5 mg/dl 3) Dave 1987 3.5-5.0 mmol/L 3.5-5.0 meq/L
				Worwag 1999 3.5 - 5.5 mmol/L (normal)
Selenium	Selenium	Serum	1) 0.74-2.97 μmol/L 58 - 234 μg/L	3) Bonaccorsi 2013 0.64-1.65 umol/L (normal) 50–130 ug/L
Sodium	Sodium	Serum	1) 136-142 mmol/L	Lowik 1992 <63ng/g 3) Dave 1987
Sounn	Sociulii	Serum	1) 136-142 mmol/L 136-142 mEq/L	135-145 mmol/L(normal) 135-145 meq/L
				Worwag 1999 136 - 146 mmol/L (normal)
Zinc	Zinc	Serum	1) 11.5-18.5 μmol/L 75-120 μg/dL	3) Bonaccorsi 2013 9.2- 17 umol/L (normal) 60–108 ug/dL
				Worwag 1999 12.2 - 23.0 umol/L (normal)

					Intervention	Control
	Design,				Change (Mean(SD))	Change (Mean(SD))
	Length,					Notations after the
Reference	Intervention	Participant Characteristics			Notations after the	numbers indicate p-
(Country)	Туре	(Age: Mean(SD))	Dosage	Biomarker	numbers indicate p-values	values
					[Mean difference btwn Int	
			[INT]		vs Ctrl]	
			D given (t0):		[@ t2]	
			600 IU/d, 4200IU/wk, or 18000		D: +47.2***	
			IU/mo		Wk: +40.7***	
				25(OH)D	Mo: +27.6***	See Intervention
			Ca given at t2 for 14 days for		D:+0.036*	
	RCT - 2		those who received vitamin D:		Wk: +0.019, NS	NS difference reported
	intervention	N=338 (76Male (M),	Dosage unclear but potentially	Ca corrected	Mo: +0.033, NS	(data not shown)
	groups,	262Female (F))	320mg or 640 mg elemental Ca		D:+0.088**	
	4.5 mo,	(N=276 completed the study)	(using CaCO3)	5	Wk: +0.065**	
	Tablet (daily or	Int:n= 166		Р	Mo: +0.017, NS	↓
Chel et al.,	weekly) or Powder	Ctrl: n= 172	[CTRL]		D:+6.0***	
2008 (Natherlands)		$A = 2^{10} 4(6.2) $	D: Placebo,	DTU	Wk: +7.7, NS Mo: +7.4*	*
(Netherlands)	(monthly	Age:84(6.3)y N=1144	Ca: Placebo	PTH	[Int vs Ctrl]	
	RCT, DB	Int:n=569			(1 year - baseline)	
	2 y,	Ctrl: n=575	[INT]	25/0100	(1  year - baseline) +17(26)***	5( <b>0</b> 0) ***
	Cod liver oil	(Treatment extended for 2	D (400 IU)	25(OH)D Ca, ionized, S		-5(28) ***
Meyer et al.,	(normal and	years: Int:n=197, Ctrl: n=186)		PTH, S	+0.003 (0.06), NS +1.0 (2.5), NS	-0.001(0.05), NS
2002	with D	,	[CTRL]	PIH, S	+1.0 (2.5), NS	+1.6(3.2), NS
(Norway) -	removed) (5ml)	Age: 84.7(7.4)y	D (20-40 IU)	OC, S	-2.92 (5.26), NS	-2.92(4.68), NS
		N=103 (103F)	[INT]		[Baseline vs final, Int vs	
		Biochem values available for	D (880 IU)		Ctrl]	
		72 participants	Ca (500 elemental as 1250	25(OH)	↑ <b>‡</b> , **	↓ ‡, ** p<0.01
	RCT, open trial	Int:34	CaCO3)	Ca	↓ NS, **	$\downarrow \ddagger, ** p < 0.01$
Krieg et al.,	(no blinding)	Ctrl: 38		PTH	↓ †,**	↑ ‡, **p<0.01
1999	2 y,	A 945(75)	[CTRL]		• 12	
(Switzerland)	Pill	Age:84.5(7.5)y	No placebo	AP (µkat/L)	$\downarrow$ b, NS p<0.01, NS	↓NS
				25(OH)D	[Baseline to final]	LNC
			[INT]	1,25(OH)2D	↑ ‡‡ ↑ NS	$\downarrow NS$ $\downarrow NS$
			D (800 IU),	1,25(OH)2D Ca	↑ NS	
		NL 2070 (2070E)	Ca (1200 mg elemental, as triCa	PTH	↓ ‡‡	→ **
		N= 3270 (3270F) Int:n=1634	phosphate)	OC (µg/L)	↓ ↓↓ ↓ NS	- NS
	RCT	Int:n=1634 Ctrl: n=1636	[CTRL]	$OC(\mu g/L)$	↓ NS	- 1ND
Chapuy et al.,	18 mo,	Cui. II-1030	D: Placebo,		$\downarrow$ NS (p<0.001 at 6 mo, p<0.01	
1992 (France)	Pill	Age:84(6)y	Ca: Placebo	AP (U/L)	(p<0.001  at 0 m0, p<0.01  at 12 m0)	↑‡
1772 (1 fance)		1.50.01(0))	Cu. 1 100000	/ ( ( ( ) L )	ut 12 mo)	1 *

## Table 5A. Supplementation: Results of Vitamin D and Calcium Studies

$ \begin{array}{c c c c c c c c c c c c c c c c c c c $				[INT]		[Trt vs ctrl]	
$ \begin{array}{ c c c c } RCT, DB & Intm=28 (6M, 22F) & (-3600 (d) & Ca Total & f ** & i $				D: 150,000 IU/mo for 2 mo, then	25(OH)D	↑ ***	↑ ***
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $				,		<b>↓</b>	
$ \begin{array}{ c c c c c c } \hline \begin{tabular}{ c c c c c c c c c c c c c c c c c c c$		· · · · · · · · · · · · · · · · · · ·		· · · · · · · · · · · · · · · · · · ·			+
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			Ctrl: n=28(6M, 22F)	+ Ca (1000 mg)	Р	↓ *	↓*
$\begin{array}{c c c c c c c c c c c c c c c c c c c $		May),					
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	2009 (Brazil)	drops/ placebo	Ctrl: 78y	+ Ca (1000 mg)	PTH, i	↓NS	↑ NS
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	al., 2011	12 wk, Pill (D only or	D only: 63 (30.1% LTC) D + Ca: 76 (53.9% LTC)	D (800 IU) alone or with	Ca	+61, no p-value +37, no p-value +0.05, no p-value +0.1, no p-value -40, no p-value	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	(Ireland)	D + Ca)	Age:77.8y	Ca (1000 mg)	PTH, i		N/A
Oct m, 2000group (Brazil)Age: 77.5 yN/AOC $1/1/1$ NS (all) $\uparrow$ NS(Brazil)12 wk, DropsAge: 77.5 yN/AOC $1/1/1$ NS (all) $\uparrow$ NSN=104 (24M, 80F) Biochem data on 77 ppt only (did not specify gender)N/AOC $1/1/1$ NS (all) $\uparrow$ NSBiochem data on 77 ppt only (did not specify gender)IINT] D (800 IU) Ca (1000 mg) $+0.097(0.106), NS$ $+0.009 (0.132), NS$ Post test 2G, 1987 (France)Ctrl: n=39ICTRL] N/APTH, i $-60.3(58.7) *$ $+18.2(92.1)*$ Post test 1G, g et al., 2010Age:83(7)yN/AUnits %) $-0.9(1.0) *$ $0(1.4)*$ Schwalfenber g et al., 2010N=68 (19 M, 49F) 8 mo),INT]INT]All subjects received supplementation for a CQI project and 94.1 % achieved at least 80 nmol/l after 5 months; unclear the		with an untreated comparison	Tr1: n=10, Tr2: n=11, Tr3: n=10	D: 7000 IU/wk, stratified by total body fat	CaT	[Tr1/Tr2/Tr3] ↑/↑/↑ † (all) ↑/↓/↑ NS (all)	↑ NS
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	· ·						1
Biochem data on 77 ppt only (did not specify gender)Biochem data on 77 ppt only (did not specify gender) $1NT]$ D (800 IU) Ca (1000 mg) $20(0H)D$ $+30(21)^{+1/2}$ $+0.00(.4)^{+1/2}$ Post test 2G, 1987 (France)Ctrl: n=39Ca (1000 mg) $PTH, i$ $-60.3(58.7) *$ $+18.2(92.1) *$ Chapuy et al., 1987 (France)6 mo, PillICTRL]Age:83(7)yN/A $AP$ (Bodansky Units %) $-0.9(1.0) *$ $0(1.4) *$ Schwalfenber g et al., 20105 - 10 mo (avg: 8 mo),Int:68IINT]IINT] $All$ subjects received supplementation for a CQI project and 94.1 % achieved at least 80 nmol/1 after 5 months; unclear the	(Brazil)	12 wk, Drops		N/A	00		† NS
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$							
$\begin{array}{c c c c c c c c c c c c c c c c c c c $				IINTI			
Int:n=38 Post test 2G, 6 mo,Int:n=38 Ctrl: n=39Ca (1000 mg)PIH, 1-60.3(58.7)*+18.2(92.1)*[Chapuy et al., 1987 (France)6 mo, PillGmo, Age:83(7)y[CTRL]AP (Bodansky Units %)-0.9(1.0) *0(1.4)*[Post test 1G, g et al., 2010N=68 (19 M, 49F) Int:68N=68 (19 M, 49F) Int:68AP (Bodansky Int:68All subjects received supplementation for a CQI project and 94.1 % achieved at least 80 nmol/1 after 5 months; unclear the			(and not speen y genaer)		-		
Post test 2G, Chapuy et al., 1987 (France)Ctrl: n=39ICTRL] (CTRL]AP (Bodansky Units %)-0.9(1.0) *0(1.4)*1987 (France)PillAge:83(7)yN/AUnits %)-0.9(1.0) *0(1.4)*1987 (France)PillAge:83(7)yN/AAll subjects received supplementation for a CQI project and 94.1 % achieved at least 80 nmol/l after 5 months; unclear theAll subjects received supplementation for a CQI project and 94.1 % achieved at least 80 nmol/l after 5 months; unclear the			Int:n=38		PTH, i	-60.3(58.7) *	+18.2(92.1)*
Chapuy et al.,6 mo,6 mo,[CTRL]AP (Bodansky1987 (France)PillAge:83(7)yN/AUnits %)-0.9(1.0) *0(1.4)*1987 (France)PillAge:83(7)yN/AUnits %)All subjects received0(1.4)*Post test 1G,N=68 (19 M, 49F)FranceFranceSchwalfenberS-10 mo (avg:Int:68Int:68Inter 5 months; unclear theSchwalfenber5 - 10 mo (avg:Int:68Int:68Inter 5 months; unclear theInter 5 months; unclear the		Post test 2G,	Ctrl: n=39	6,			
Post test 1G,       N=68 (19 M, 49F)         Schwalfenber       5 - 10 mo (avg: g et al., 2010         8 mo),       [INT]	Chapuy et al.,			[CTRL]	AP (Bodansky		
Post test 1G, g et al., 2010N=68 (19 M, 49F)supplementation for a CQI project and 94.1 % achieved at least 80 nmol/1 	1987 (France)	Pill	Age:83(7)y	N/A	Units %)		0(1.4)*
		5 - 10 mo (avg:		INTI		supplementation for a CQI project and 94.1 % achieved at least 80 nmol/1	
	(Canada)	Pill	Age: 80.7(9.8)y	D (2000 IU)	25(OH)D	change from baseline	

INT = Treatment Intervention, Ctrl = Control; NS = non-significant; N/A = not applicable; S= Serum. Interventions are daily dose unless otherwise stated. **RCTc**(RCT-Crossover), RCT (RCT-parallel: randomized, 2 groups or more; 1 control/comparison), Pre/Post C (Pre-test/Post-test comparison- has comparison group), non-randomized trial (e.g. 1 nursing home with treatment, another without), Pre/Post 1G (Pre-test/post-test 1 group – 1 group), Post 2G (Post-test – 2 group comparison), Post 1G (Post-test – 1 group); DB= double blind. Baseline vs final:  $\dagger p < 0.05$ ,  $\ddagger p < 0.01$ ,  $\ddagger p < 0.001$ ; Intervention vs Control:  $\ast p < 0.05$ ,  $\ast \ast p < 0.001$ . **DOSAGE UNITS:** A, D: (IU); E, C, B1, B2, B3, B5, B6, Ca, Cu, Fe, I, K (potassium), Mg, Zn: (mg); Folic acid, B7 (biotin) B12, Mo, Mn, Se: (µg); assumed vitamin E as dl-alpha-tocopherol (synthetic form). **BIOMARKER UNITS: D/Ca:** 25(OH)D (nmol/L), 1,25(OH)2D (pmol/L), Ca (mmol/L), PTH (ng/L), OC (µg/L), P (mmol/L), PTH, i (ng/L), AP (Bodansky Units %), AP (µkat/L), AP (µg/mL), Alb (g/L) **Others:** A (µmol/L), 25(OH)D (nmol/L), C (µmol/L), B1 (aETK), B1 (Erythrocyte TPP) (µmol/L), B1 (TPP (nmol/L), B2 (aEGR), B6 (aEAST), Folate (nmol/L), B12, S (pmol/L), Cu(µmol/L), Zn (µmol/L); MMA, S (µmol/L), HCys, S (µmol/L), Hemotocrit (% RBC), Mean corpuscular volume (fl)

Author	Design, Length,			Biomarker	Intervention	Control
(Country)	Intervention Type	Participant Characteristics	Dosage	Biomarker	Change	Change
			Multi-nutrient			
			[INT]	А	↑ ‡‡	↑NS
			Vitamins: A (2,666), D	D3	↑ ‡‡	↑NS
			(400), E (60), B1 (1.2), B2	Е	↑ ‡‡	↓NS
			(1.4), nicotinamide (14), Ca	С	↑ ‡‡	↑ NS
			pantothenate (5), B6 (3.0),	Folate	↑ ‡‡	↓NS
			B7 (30), folic acid (600),	Cu	- NS	↑ NS
		N=119	B12 (200), C (120)	Se	↑ <b>‡</b> ‡	↑NS
Allsup et al., 2004 (UK) [REF]		Int:n=61 (25M, 36 F) Ctrl: n=57 (18M, 39F) Note: 1 participant dropped out	<b>Minerals:</b> Ca (240), Cu (2000), Fe (12), I (150), Mg (100), Mo (100), Se (60), Zn (14)			
	RCT, DB, placebo	Age§				
§ median	8 wk,	Int: 82.6(8.8)y	[CTRL]			
(IQR)	Pill	Ctrl: 83.1(6.6)y	Placebo	Zn	↑ NS	- NS
				E (a- tocopherol) C (ascorbic acid) B1 (aETK) B1	$M :\uparrow \dagger, *$ $F: \uparrow NS, *$ $M: \uparrow \dagger, *$ $F: \uparrow \dagger, *$ $M: \downarrow NS, NS$ $F: \downarrow \dagger, *$	$\begin{array}{c} M:\uparrow NS, *\\ F:\uparrow NS, *\\\\ M:\uparrow NS, *\\\\ F:\downarrow NS, *\\\\ M:\uparrow NS\\\\ F:\downarrow NS \end{array}$
			[INT]	(Erythrocyte	M:↑ †,*	M: ↑ NS*
	RCT, stratified by	N=84 (31M, 53F)	Vitamin E (6.8), C (200),	TPP)	F:↑ †,*	F:↑NS*
	gender, DB	Int:n=43(16M, 27F)	B1 (7.5), B2 (9), B3 (35),		M:↓ †,*	M:↑NS*
Asciutti-	placebo	Ctrl: n=41 (15M, 26F)	B5 (15), B6 (11)	B2 (aEGR)	F:↓ †,*	F: - NS*
Moura et al.,	30 d,		[CTRL]		M:↓ †,*	M:↓NS*
1993 (France)	Pill	Age: >65 y	Placebo	B6 (aEAST)	F:↓ †,*	F: ↑ NS*
			[INT] Vitamins: A (900, B- carotene), D (400), E	25(OH)D	+27.4(3.9) *** [% Cut-off ]	-6.0(2.1)***
			(12.2), C (75), B1 (15), B2	$\% \le 50$	↓ NS	↑ NS
	RCT, DB, placebo, matched treatment	N=92 Int:n=49	(12.2), C (75), B1 (15), B2 (10), Nicotinamide (50), B5 (35 as Ca pantothenate), B6	% >50	↑ ***	J ***
Grieger et al.,	and control on age;	Ctrl: n=43	(25), B7 (100), Inositol (8),	Folate	+13.0(1.6)***	-0.4(2.3)***
2009	24 wk,		Folic acid (200), B12 (25),	% ≤ 7	↓ ***	↑ ***
(Australia)	Pill	Age:	Choline bitartrate (7.9 as	%>7	↑ NS	1 NS

## Table 6A. Supplementation: Results Other Micronutrient Studies

			Choline bitartrate)	B12	+145.6(33.1)***	-32.4(30.2)***
			Minerals: Ca (144	% ≤ 200	***	↑ ***
			elemental; 360 as CaCO3),		*	
			Fe (5 elemental, 15.2 as ferrous fumarate), Mg (75	%>200	↑ NS	↓NS
			elemental, 125 as Mg2O3),			
			Mn (750 elemental, 7.5 mg			
			as Mn amino acid chelate),			
			K (1.5 elemental; 3.4 as K sulphate), Zn (6 elemental,			
			30 as Zn amino acid			
			chelate) 6mg (30mg)			
			Others: Bioflavonoids,			
			Siberian ginseng			
			[CTRL]			
			Placebo	Zn	-0.1(0.5) NS	+0.1(0.4) NS
				E nl	* ++	↑NS
				E, pl	↑ ‡‡	1\\S
				А	[% deficient]	
				(Carotenoid)	0 NS, NS	+6 ↑ NS, NS
				А	+1↑ †, NS	+2 ↑ †, NS
			[INT] Vit E (90) + 50% RDA of	D	-2↓ †, NS	-2↓†, NS
			other essential vitamins and	Е	-3↓ NS, NS	-1↓ NS, NS
			minerals	B1	+2↑ NS, NS	-4↓ NS, NS
			Vitamins: A (1332 IU), D	B2	2↑ NS, NS	0- NS, NS
			(4000), C (30), B1 (0.6), B2 (0.6), B3 (6.0), B6 (0.9),	B6 (P5P)	-4↓ †, NS	-4↓ †, NS
			folic acid $(100)$ , B12 $(1)$	B12	0 NS, NS	0- NS, NS
				Folate	0 NS, NS	0- NS, NS
		N 417	<b>Minerals:</b> Cu (0.8), Fe (5),	Cu	-3↓ NS, NS	+4↓ NS, NS
		N=617 Int:n=311	I (75), Se (25), Zn (7)	Fe (Ferritin)	0 NS, NS	0- NS, NS
	RCT, DB, placebo	Ctrl: n=306	[CTRL]	Zn	0 NS, NS	+3↑ NS, NS
Meydani et	1 yr,		Vit E $(1.8 \ \mu g)$ + Remaining	Alb	+9↓ †, *	+12↑ †, *
al., 2004 (US)	Pill (soybean oil)	No age info given	Vit/Min as Intervention	Hb	-1↓NS*	+6↑ NS*
	RCT, DB, placebo		[INT] Vitoming	A (B- carotene)	(V/M/V+M) $\uparrow/\downarrow/\uparrow$ NS all	
Monget et al.,	controlled, age and gender stratified; 3	N=575 (153M, 422F)	<b>Vitamins:</b> A (20 = 1000 RE, B-	A (Retinol)	$\uparrow/\downarrow/\uparrow$ NS all	↓ 
1996 (France)	treatment groups	No Trt/Ctrl breakdown	carotene), E (15, a-	E (a-	Ι, ψ/   1 τος απ.	•
	6 mo,	Age: 82.9(7.8)y	tocopherol), C (120)	tocopherol)	$\uparrow/\uparrow/\uparrow$ Sig V effect	$\downarrow$

	Pill			С	↑/↓/↑ Sig V effect	↑
			Minerals: Se (100		$\uparrow/\uparrow/\uparrow$ Sig M effect, Sig V+M	
			elemental, in sodium	Se	interaction	1
			selenite), Zn (20 elemental,			
			in zinc sulfate)			
			Vit-Min: contains both			
			vitamin/mineral content			
			[CTRL]			
			Placebo	Zn	-/↑/↑ Sig M effect	1
	I		Single Nutrient			•
					[Change difference]	
				B12, S	101.6 (60.1 - 143.2) ***	
		N=50			-0.13 (-0.19 to	
		Int: n=26 (12M,14F)		MMA	-0.06) ***	
		Ctrl: n=24 (11M,13F)	[INT]	Hava	$0.04(1.2 \pm 0.1.2)$ NS	
			B12 (1000 μg)	Hcys	0.04 (-1.2 to 1.3), NS	
Favrat et al.,	RCT,	Age:		Hct	-0.4 (-1.7 to 0.8), NS	
2011	4 wk,	Int:69.6(18.8)y	[CTRL]	MOU		
(Switzerland)	Pill	Ctrl: 68.6(18.5)y	Placebo	MCV	-0.4 (-2.2 to 1.4) NS	See intervention
		N=88	[INT]			
T	DCT DD alasha	Int: n=43	C (1000)			
Ter Riet et al., 1995 (The	RCT, DB, placebo 12 wk,	Ctrl: n= 45				
Netherlands)	IZ WK, Pill	No ago info given	[CTRL] C (20)	Cnl	- 64.2 No p values	+5.11
ineuterialius)	F 111	No age info given N=43(18M, 25F) for baseline	C (20)	C,pl Zn, S	+ 64.2, No p-values ↑ ‡	+3.11 N/A
		data;			+	
		Only 15 participants on				
Arcasoy et	Pre/Post1G	supplements				
al., 2001	90 d,	supplements	Zn (30) (elementary, in	Zn Binding		
(Turkey)	Pill	No age info given.	ZnSO4 formula)	capacity, S	↓ ‡	

See Table 6A notations; Baseline vs final:  $\dagger p < 0.05$ ,  $\ddagger p < 0.01$ ,  $\ddagger p < 0.001$ ; Intervention vs Control:  $\ast p < 0.05$ ,  $\ast \ast p < 0.01$ 

	Design,					Intervention	Control
Author	Length	Food; Svg Size	Participant Characteristics	Intervention	Biomarker	Change	Change
					25(OH)D, S	~+7.5 † ~ -3, NS (but significant	_
Bonjour et al.,	RCTc,	Cheese;	N=21 (21F)	[INT] D (100)	PTH , S	reduction compared to control, per text)	
2011 (France)	6 wk	2x100g svg/d	Age: 87.2(6.1)y	Ca (302)	OC,S	~2 µg/L, NS	N/A
			N=59 Int: n=32F			[p-value group diff]	
			Ctrl: n=27F	[INT] D (400),	25(OH)D	+25.3(1.8) ***	+5.2(2.5)***
	RCT,			Ca (800)	Ca P, i	- NS +0.08(0.03) NS	-0.03(0.02) +0.10(0.02)
	DB,	Yogurt; 250g	Age:		PTH	-28.6(7.2) **	-7.1(2.9)**
Bonjour et al., 2013 (France)	placebo 56d	(2x125g svg/d)	Int:85.8(1.2)y Ctrl:85.1(1.3)y	[CTRL] Ca (280)	AP μg/L	-1.4(1.4), NS	-0.1(1.2) NS
					25(OH)D, S* Ca, S	↑ ‡‡ ↓ NS	_
Mocanu et al., 2009 (Romania)					Ca, U	↓ ‡‡ (significance also seen at 3 and 6 mo)	
*Used paper values - paper different from abstract for	Pre/Post 1G,	Bun; 100g, 1	N=45 (17 M, 28F)	[INT] D (5000), Ca (320 elemental,	PTH, S	↓ ‡‡ (significance also seen at 6 and 9 mo)	-
25(OH)D	1 yr	svg/d	Age: 71(6.9)y	800 as CaCO3)	OC, S	↓ <b>‡</b> ‡	N/A
(011)2		6			25(OH)D, S Ca, S	++++ +2 ‡ -0.02 NS	
					P, S	+0.03 NS	-
					Alb, S	+2.1 ‡‡	
	Pre/post	Chasse	N=35 (35F)	[INT]	PTH, S	-9.2 ‡	-
Bonjour et al., 2009 (France)	1G, 1 mo	Cheese; 2x100g svg/d	Age: 84.8(8.1)y	D (100) Ca (302)	OC, S AP, S µg/ml	+2.7 † +0.1 NS	N/A
		2X100g 3Vg/u		Ca(502)		T0.1 105	11/71

Table 7A. Fortification: Results from Vitamin D and Calcium Studies

See Table 6A notations; Baseline vs final: † p<0.05, ‡ p<0.01, ‡‡ p<0.001; Intervention vs Control: \*p<0.05, \*\*p<0.01, \*\*\*p<0.001

	Design,	Participant	Food; Svg Size	Dosage level (total daily)		Intervention	Control
Authors	Length	Characteristics		•	Biomarker	Change	Change
				[INT] C (31.5), B1 (0.44),	С	+ 17(25)*	+ 14(25)*
		N=33 (33F)	Int: Fortified fruit	B6 (0.81),	B1 (TPP)	+16(21)**	-22(43)**
		Int: n=15	juice w 50g CHO +	Folic acid (63),	B6 (P5P)	+ 45(24)***	-1(21)***
		Ctrl: n=18	50% of dietary	B12 (1.10)	Folate	+6(5), NS	+3(9), NS
Van der			recommendations of		B12	-11(131), NS	-22(114), NS
Wielen et al., 1995 (The Netherlands)	RCT, single blind, placebo 12 wk	Age: Int:81(6)y Ctrl: 82(8)y	water-soluble vitamins, 400ml (2x200ml/d)	[CTRL] Placebo juice with C (40.5)	Hcys	-7(8)*	+2(12)*
(tetricitatios)	12 WK	Cull. 02(0)y	400111 (2x200111/d)	[INT]	The ys	-7(0)	12(12)
				Trt 1: 200 µg Food	Folate, S	↑ ‡‡, *	↓ NS, *
				folate + 200 $\mu$ g	Folate, RBC	↑ <del>*</del> * *	↑ <b>* * *</b>
				folic-acid fortified	Hb	↑ NS,*	↑ <b>**</b> ↑ <b>**</b>
Bermejo et al., 2009 (Spain) Using				margarine (400 µg total folic acid)			
Centre M and	Pre/Post C,	N=126	Margarine,	[CTRL]			
C data only	6 mo	Age: 82.4(7.3)y	10 g portion	Placebo	Hcys	↓ NS, NS	↓ NS, NS
				[INT]	25(OH)D), S	↑‡	
				D (640), E (16), C	Folate, S	↑‡	
			Pureed food -	(180), B1 (1.6), B2			
Adolphe et			vegetable and meat at	(2.0), B3 (21), B5			
al., 2009	Pre/Post 1G,	N=11 (2M, 9F)	lunch and supper;	(2.4), B7 (30), folic	DIA G	4.310	37/4
(Canada)	8 wk	Age: $\geq 50y$	400g (4 x100g svg/d)	acid (400), B12 (4)	B12, S	↑ NS	N/A
		N=89			E-1-4- C	No baseline	N
		Int:49 (10M, 39F) Ctrl: 40 (10M, 30F)		[INT]	Folate, S	given, ***	No baseline ***
		Cuii. 40 (101vi, 50F)		Folic acid (76)			
		Age:	Milk,	1011c acid (70)			
Keane et al.,	Post test 2G	Int:84y	200ml(2x100ml)	[CTRL]		No baseline given	
1998 (Ireland)	6 mo minimum	Ctrl: 81.9y	svg/d)	Folic acid (8)	Folate, RBC	***	No baseline ***

### Table 8A. Fortification: Results of Other Micronutrient Studies

See Table 6A notations; Baseline vs final: † p<0.05, ‡ p<0.01, ‡‡ p<0.001; Intervention vs Control: \*p<0.05, \*\*p<0.01, \*\*\*p<0.001

Reference (Location)	Biomarkers	<b>Baseline - Int</b> [Mean(SD), unless otherwise indicated]	Endpoint – Int	Baseline – Ctrl	Final – Ctrl
	25(OH)D (nmol/L)	D: 23.0(8.3) Wk: 27.3(12.7) Mo: 23.8(8.0)	[@ t2] D: 69.9(17.8) Wk: 67.2(14.0) Mo: 53.1(15.9)	25.2(12.1)	[@ t2] 25.5(12.0)
	Ca corrected (mmol/L)	D:2.42(0.10) Wk: 2.41(0.08) Mo: 2.42(0.09)	D:2.45(0.10) Wk:2.43(0.10) Mo:2.44(0.10)	2.42(0.10)	2.42(0.09)
	P (mmol/L)	D:1.01(0.14) Wk:1.03(0.15) Mo:1.02(0.13)	D:1.05(0.11) Wk:1.04(0.14) Mo:1.04(0.12)	1.04(0.12)	1.01(0.14)
Chel et al., 2008 (The Netherlands)	PTH (ng/L) (ratio of medians)	D:66.4(45.5-107.3) Wk:59.1(48.2-86.4) Mo:65.5(46.4-99.1)	D:46.4(33.6-70) Wk:53.6(47.3-69.1) Mo:50.9(39.1-80.9)	65.5(45.5-107)	68.2(46.4-100)
	25(OH)D, S (nmol/L)	47(26) (n=34)	(@ End of 1 year - No data available on Year 2) 64(21)	51(33) (n=31)	(@ End of yr 1 - No data on yr 2) 46(20)
Meyer et al.,	Ca, ionized, S (mmol/L)	1.23(0.05) (n=31)	1.23(0.06)	1.24(0.04) (n=26)	1.24(0.06)
2002 (Norway) Krieg et al.,	PTH, S (ng/L) OC, S (µg/L) 25(OH)D (nmol/L)	6.5(3.1) (n=36) 12.3(5.85) (n=35) 29.7(3.0)	7.5(4.2) 9.36(4.68) 66.1(4.0)	5.6±3.3 (n=34) 11.7(5.26) (n=33) 29.2(3.0)	7.2(4.7) 8.77(4.09) 14.2(2.5)
1999 (Switzerland	Ca (mmol/L) PTH (ng/L)	$2.32 \pm 0.02$ $43.1 \pm 3.2$	$ \begin{array}{r}       2.31 \pm 0.02 \\       35.5 \pm 2.7 \end{array} $	$2.29 \pm 0.01$ $44.6 \pm 3.5$	$   \begin{array}{r}     14.2(2.3) \\     2.23 \pm 0.01 \\     67.2 \pm 5.7 \\   \end{array} $
)	AP (μkat/L) 25(OH)D (nmol/L)	1.47(0.09) 39.9(27.5)	1.26(0.09) 104.8(22.4)	1.45(0.08)           25.0 (20.0)	1.40(0.09) 27.5(17.5)
	1,25(OH)2D (pmol/L) Ca (mmol/L)	67.6(26) 2.29(0.09)	70.2(23.4) 2.30(0.1)	75.4(26)	67.6(23.4) 2.25(0.09)
Chapuy et al., 1992	PTH (ng/L) OC (µg/L)	54(37) 8(3)	30(14) 7(2)	50(24) 8(3)	56(29) 8(3)
(France) Moreira-	AP (µkat/L) 25(OH)D (nmol/L) Ca, ionized	1.15(0.42) 45.9 (20.3–84.8)	1.12(0.37) 86.6 (52.3–106.5)	1.20(0.37)           39.5 (20.3-68.8)	1.49(0.45) 51.8 (23.5–107.8)
Pfrimer et al., 2009 (Brazil)	(mmol/L) Ca T (mmol/L)	1.3 (1.2–1.4) 2.23(1.98 - 2.48)	1.25 (1.17–1.36) 2.27(2.08-2.45)	1.3 (1.2–1.4) 2.25(1.85-2.35)	1.27 (1.17–1.41) 2.23(1.82-2.50)
(median (ranges)	P (mmol/L) PTH, i (ng/L)	1.13(0.84-1.52)       48.5 (42.3-158.1)	1.10(0.87-1.42) 41.4 (21.6–151.6)	1.13(0.74-1.45)       45 (20.7-162.7)	$\frac{2.25(1.62-2.50)}{1.10(0.87-1.55)}$ $47.5(6.6-101.5)$
Dinizulu et al., 2011	25(OH)D (nmol/L) Ca (mmol/L)	[D only/ D+Ca] 24.4/ 27.2 2.25/2.25	[D only/ D+Ca] 84.5/63.6 2.33/2.35		
(Ireland)	PTH, i	not reported [Tr1/Tr2/Tr3]	not reported	N/A	N/A
	25(OH)D (nmol/L)	46.9(16.0)/ 55.9(26.7)/ 60.4(18.5)	62.4(15)/ 76.1(16.2)/ 80.6(17.5)	61.2(17.7)	54.4(23)
	Ca T (mmol/L)	2.20(0.07)/2.20(0.1)/ 2.1(0.1)	2.23(0.05)/ 2.20(0.05)/ 2.20(0.07)	2.20(0.07)	2.23(0.05)
	PTH (ng/L)	58.6(17.5)/ 51.2(28.1)/ 53.6(28.6)	57.2 ± 30.5/ 52.8 ± 25.4/ 50.1 ± 25.1	29.6(8.2)	36(12.2)
Canto-Costa et al., 2006 (Brazil)	OC (µg/L)	$26.2 \pm 8.1/40.2 \pm 22.8/34.5 \pm 14.2$	$35.1 \pm 18.1/40.9 \pm 20.8/33.9 \pm 16.6$	25.6(8.6)	27.1(8.1)

Table 5B. Supplementation: Results from Vitamin D and Calcium Studies

Chapuy et al., 1987 (France) Schwalfenbe rg et al., 2010	25(OH)D (nmol/L) Ca (mmol/L) P (mmol/L) PTH, i (ng/L) AP (Bodansky Units %)	21(11) 2.25(0.11) 1.09(0.01) 75.0(99.4) 4.6(1.3)	No final values - Only change in values given (See Table 1A) (≥5 mo)	Same as Trt baseline	No final values - Only change in values given (See Table 1A)
2010 (Canada)	25(OH)D (nmol/L)	N/A	(≥5 mo) 119.4(28.1)	N/A	N/A

D (IU), Ca (mg); NS = non-significant; N/A = not applicable; \*Daily dose unless otherwise stated

Author	Biomarkers	Baseline - Int - 1st Arm?	Endpoint - Int	Baseline - Ctrl	Final - Ctrl
			Multi-nutrients		
	A (µmol/L)	2.9(0.9)	3.2(1.0)	3.1(1.0)	3.2(1.2)
	D (nmol/L)§	32.4(12.5)	52.4(22.5)	54.0(30.6)	49.5(27.0)
	E (µmol/L)	25.4(8.8)	35.7(13.2)	29.2(10.5)	29.1(10.9)
Allsup et al.,	C (µmol/L)§	16.2(20.3)	58(31.5)	17.6(25.2)	23.9(20.2)
2004 (UK)	Folate (nmol/L)§	10.6(12.5)	27.4(17.7)	10.2(7.92)	9.74(9.06)
[REF]	Cu(µmol/L)	20.0(3.7)	20.0(3.8)	19.4(4.1)	19.6(4.1)
§ median	Se (µmol/L)	1.04(0.22)	1.16(0.22)	1.04(0.23)	1.06(0.26)
(IQR)	Zn (μmol/L) E (a-tocopherol) (μmol/L)	10.3(1.6) M:19.3(4.57) F:22.8(24.21)	10.6(1.8)           M: 27.9(4.85)           F: 24.4(7.32)	10.7(2.1)           M: 15.1(0.52)           F:19.1(6.54)	10.7(2.0) M: 16.2(8.25) F: 19.3(6.45)
	C (ascorbic acid) (µmol/L)	M:26.8(22.12) F:36.8(27.42)	M:85.2(15.68) F:96.6(18.65)	M:24.2(19.35) F:31.2(9.87)	M:23.0(23.5) F:28.4(16.42)
	B1 (aETK))	M:1.16(0.10) F: 1.13(0.13	M:1.05(0.09) F:1.06(0.09)	1.12(0.12)/1.11(0.10)	1.13(0.09)/1.10(0.12)
	B1 (Erythrocyte TPP) (µmol/L)	M:0.30(0.062) F:0.19(0.056)	M:0.35(0.041) F: 0.30(0.086)	0.21(0.058)/0.24(0.065)	0.23(0.082)/0.26(0.086)
Asciutti- Moura et al.,	B2 (aEGR)	M:1.10(0.12) F: 1.07(0.09)	M:1.05(0.04) F:1.04(0.03)	1.08(0.10)/1.07(0.09)	1.10(0.10)/1.07(0.08)
1993 (France)	B6 (aEAST)	M:1.85(0.40) F: 1.88(0.40)	M:1.70(0.25) F:1.60(0.15)	1.88(0.32)/1.85(0.28)	1.85(0.31)/1.89(0.31)
	25(OH)D (nmol/L)	35.7(2.8)	No final MN values, only change	35.5(2.5)	No final MN values, only change
	[Cut-off ranges] % ≤ 50 nmol/L	(77%, n=37)	(23%, n=11)	(83%, n=35)	(90%, n=38)
	% >50 nmol/L	(23%, n=11)	(77%, n=36)	(17%, n=7)	(10%, n=4)
	Folate (nmol/L)	14.8(1.4)	No final MN values, only change	19.0(2.0)	No final MN values, only change
	$\leq$ 7 nmol/L	(14%, n=6)	(0%, n=0)	(13%, n=4)	(21%, n=9)
	>7 nmol/L	(86%, n=36)	(100%, n=47) No final MN values,	(87%, n=28)	(79%, n=33) No final MN values,
	B12 (pmol/L)	273.8(17.8)	only change	296.0(25.0)	only change
	$\leq 200 \text{ pmol/L}$	(30%, n=13)	(6%, n=3)	(31%, n=10)	(40%, n=17)
	>200 pmol/L	(70%, n=30)	(94%, n=44)	(69%, n=22)	(60%, n=25)
Grieger et al., 2009 (Australia)	Zn (µmol/L) (No cut-offs given)	11.6(0.5)	No final MN values, only change	10.6(0.3)	No final MN values, only change
	E, pl (µmol/L)	26.5(9.07)	49.2(16.0)	26.7(9.96)	28.1(9.47)
	A (Carotenoids)	[% deficient] 11	11	6	12
	A	1	2	2	4
	D E	2 3	0 0	2	0 0
Mandar: -+	B1	0	2	4	0
Meydani et al., 2004	B1 B2	0	2	2	2
(US)	B6	10	6	9	5

**Table 6B.** Supplementation: Results Other Micronutrient Studies

	B12	0	0	0	0
	Folate	0	0	0	0
	Cu	6	3	7	3
	Fe (Ferritin)	0	0	0	0
	Zn	48	42	50	53
	Alb	19	28	27	39
	Hb	32	31	37	43
		(V/M/V+M)	(V/M/V+M)		
	A (B-	0.90(0.53)/0.88(0.51)/	2.95(1.68)/0.84(0.54)/		
	carotene)(µmol/L)	0.87(0.54)	3.20 (1.83)	0.83(0.53)	0.75(0.37)
	A (Retinol)	2.10(0.63)/2.00(0.61)/	2.14(0.69)/2.10(0.69)/		
	(µmol/L)	2.01(0.63)	2.08(0.66)	2.06(0.73)	1.96(0.63)
	E (a-tocopherol)	29.9(7.85)/	35.1(8.43)/29.6(8.68)/		
	(µmol/L)	29.5(8.89)/29.3(7.38)	34.3(8.41)	30.2(8.64)	30.0(0.801)
		16.8(18.6)/19.6(18.1)/	47.3(18.6)/18.7(18.9)/		
	C (µmol/L)	18.91(18.91)	48.94(18.91)	19.1(18.3)	32.82(6.64)
		0.72(0.19)/	0.77(0.25)/1.18(0.20)/		
Monget et	Se (µmol/L)	0.73(0.19)/0.70(0.20)	1.11(0.23)	0.73(0.54)	0.74(0.20)
al., 1996		10.7(1.95)/10.7(1.98)/	10.7(2.17)/11.0(2.17)/		
(France)	Zn (µmol/L)	10.93(2.22)	11.11(2.31)	10.69(1.94)	10.59(2.10)
			Single Nutrient		
	Folate, S	[Post Int (1 mo)]		[Post Int (1 mo)]	
	(nmol/L)	16.6(9.1)	No final values	19.2(10.9)	No final values
	í í				
	B12, S (pmol/L)	164(24)	263.4(89.8)	154(20)	154.5(41.1)
	MMA, S				
	(µmol/L)	0.43(0.25)	0.23(0.08)	0.41(0.24)	0.37(0.14)
	HCys, S (µmol/L)	18.3(6.6)	16.5(6.1)	15.0(5.3)	13.9(4.3)
	Hemotocrit (%				
	RBC)	40.3(4.2)	39.6(4.1)	39.5(4.6)	39.7(4.6)
	Mean corpuscular				
Favrat et al.,	volume (fl)	91.2(9.2)	89.8(6.9)	92.6(5.1)	92.8(7.0)
2011	Creatinine, S				
(Switzerland)	(µmol/L)	96.4(27.9)	No final values	89.0(27.2)	No final values
Ter Riet et					
al., 1995					
(The		No baseline values		No baseline values	
	1 (1) (1) (1)	given	84.6	given	27.3
	C, pl (µmol/L)	8			
		12.96(0.94)	14.34 (1.18)		
Netherlands)	Zn, S (µmol/L)	<u> </u>	14.34 (1.18)		
Arcasoy et al., 2001		<u> </u>	14.34 (1.18)	_	

Units used: A, D: (IU); E, C, B1, B2, B3, B6, Ca, Cu, Fe, I, K (potassium), Mg, Zn: (mg); Folate, B7 (biotin) B12, Mo, Mn, Se: (µg)

Author	Biomarkers	Baseline - Int	Final - Int	Baseline-Ctrl	Final-Ctrl
	25(OH)D, S				
	(nmol/L)	21.96(18.72)			
	Ca, S (mmol/L)	2.24(0.07)	Statistically significant increase in 25(OH)D,		
	P, i, S (mmol/L)	1.12(0.12)	and significant decrease in PTH between		
	PTH, S (ng/L)	75.8(24.2)	intervention and		
	Alb, S (g/L)	31.8(2.7)	control. No significant differences were		
Bonjour et al.,	Creatinine , S (µmol/L)	83.9(25.9)	recorded between the intervention and control		
2011 (France) – Crossover	OC, S (μg/L)	30.3(13.0)	period for serum Ca, P, Alb, and AP (data not		
control	AP, S (µg/mL)	13.6(5.3)	shown).	N/A	N/A
	25(OH)D (nmol/L)	19.2(1.2)	[@ d56] 44.6(2.5)	16.2(0.6)	[d56] 21.4(2.7)
	Ca (mmol/L)	2.31(0.02)	2.31(0.02)	2.31(0.02)	2.29(0.02)
	P, i (mmol/L)	1.17(0.03)	1.24(0.03)	1.14(0.03)	1.24(0.03)
Bonjour et al.,	PTH (ng/L)	60.8(7.1)	32.4(1.8)	53.4(6.3)	46.3(4.6)
2013 (France)	AP ( $\mu g/L$ )	18.9(1.2)	17.5(1.8)	20.2(1.2)	17.5(1.8)
	25(OH)D, S				
	(nmol/L)	28.5(9.9)	126.4(37.3)		
	Ca, S (mmol/L)	2.29(0.15)	2.28(0.15)		
	Ca, Urine				
Mocanu et al.,	(mmol/L)	3.7(1.6)	3.4(2.2)		
2009	PTH, S (pg/mL)	59.3(38.2)	19.0(16.0)		
(Romania)	OC, S ( $\mu$ g/L)	20.1(10.3)	14.7(9.0)	N/A	N/A
	25(OH)D, S				
	(nmol/L)	13.73(4.24)	15.72(4.24)		
	Ca, S (mmol/L)	2.29(0.09)	2.27(0.11)		
	P, S (mmol/L) 1.18(0.12)		1.21(0.16)		
	Alb, S (g/L) 33.9(2.7)		36.0(2.6)		
	PTH, S (ng/L) 74.9(22.6)		65.7(23.7)		
	OC, S (µg/L)	32.6(14.6)	35.3(17.5)		
	AP, S (µg/ml) -				
Bonjour et al.,	need to convert				
2009 (France)	U/L to ukat/L	16.4(10.1)	16.5(13.8)	N/A	N/A

**Table 7B.** Fortification: Results from Vitamin D and Calcium Studies

D (IU), Ca (mg); NS = non-significant; N/A = not applicable; \*Daily dose unless otherwise stated

		Baseline (Biochemical	Final (Biochemical status)		
Authors	Biomarkers	(blochennear Status) - Int	- Int	Baseline - Ctrl	Final - Ctrl
	C (µmol/l)	33(28)		20(14)	
	B1 (TPP)				
	(nmol/L)	131(26)		149(42)	
	B6 (P5P)				
	(nmol/L)	39(16)		46(25)	
	Folate				
Van der	(nmol/L)	10(5)		14(11)	
Wielen et al.,	B12 (pmol/L)	320(202)	No final values; Only	365(224)	No final values;
1995 (The	Hcys		change given (see Table		Only change given
Netherlands)	(µmol/L)	18(8)	4A)	17(5)	(see Table 4A)
	Folate, S	[Centre M]		[Centre C]	
	(nmol/L)	16.6 (6.1)	27.1(9.4)	14.6(5.9)	14.5(5.3)
	Folate, RBC				
	(nmol/L)	748 (260)	1403(438)	588 (416)	902(175)
Bermejo et	Hb (g/L)	129(14)	132(17)	131(16)	142(14)
al., 2009	Hcys				
(Spain)	(µmol/L)	16.1 (5.4)	14.9(4.4)	18.0(5.2)	17.0(4.8)
	25(OH)D, S				
	(nmol/L)	41(21)	66(11)	_	
	Folate, S				
Adolphe et	(nmol/L)	10.7(4.9)	25.2(6.4)	-	
al., 2009	B12, S				
(Canada)	(pmol/L)	436(192)	448(111)	N/A	N/A
	Folate,S	No baseline			
	(nmol/L)	given	13.17(8.18)	No baseline given	4.89(4.49)
Keane et al.,	Folate, RBC	No baseline			
1998 (Ireland)		given	717.26(316.38)	No baseline given	444.39(230.18)

**Table 8B.** Fortification: Results from Other Micronutrient Studies

Units used: A, D: (IU); E, C, B1, B2, B3, B6, Ca, Cu, Fe, I, K (potassium), Mg, Zn: (mg); Folate, B7 (biotin) B12, Mo, Mn, Se: (µg)

<b>Reference</b> (Country)	Dose (daily, unless otherwise specified)
	D 600 IU/d, 75% RDA)
	[Or 4200IU/wk, or 18000IU/mo]
	Or
Chel et al., 2008 (Netherlands)	Ca (320 mg, 27% RDA) with D (3 dosage schedules, above)
Meyer et al., 2002 (Norway)	D (400 IU, 50% RDA)
Meyer et al., 2002 (Norway)	D (400 10, 30% KDA)
	D (880 IU, 110% RDA)
Krieg et al., 1999 (Switzerland)	Ca (500 mg elemental calcium, 42% RDA)
	D (800 IU, 100% RDA)
Chapuy et al., 1992 (France)	Ca (1200 mg, 100% RDA)
	150,000 IU and 90,000 IU vitamin D per month for a 6 month intervention
Moreira-Pfrimer et al., 2009 (Brazil)	(~3667 IU, 306% RDA)
	D (800 IU, 100% RDA) alone OR withwith
Dinizulu et al., 2011 (Ireland)	Ca (1000 mg, 83% RDA)
Canto-Costa et al., 2006 (Brazil)	D(7000  III/wk 1250) DDA at 1000 III/day)
Canto-Costa et al., 2000 (DIaZII)	D (7000 IU/wk, 125% RDA at 1000 IU/day)
	D (800 IU, 100% RDA) and
Chapuy et al., 1987 (France)	Ca (1000 mg, 83% RDA)
Schwalfenberg et al., 2010 (Canada)	D (2000 IU, 167% RDA)

#### RDAs/AIs for Male/Females >70 years of age:

Vitamins A (900/700 µg), vitamin D (800 IU), E (15/15 mg), C (90/75 mg), thiamin (1.2/1.1 mg), riboflavin (1.3/1.1 mg), niacin (16/14 mg), pantothenic acid (5/5 mg, AI used), B6 (1.5/1.5 mg), folate (400/400 µg), B12 (2.4/2.4 µg), biotin (30/30 µg, AI used), choline (550/425 mg, AI used); calcium (1200/1200 mg), copper (900/900 µg), iodine (150/150 µg), iron (8/8 mg), magnesium (420/320 mg), manganese (2.3/1.8 mg, AI used), potassium (4700/4700 µg, AI used), selenium (55/55 µg), and zinc (11/8 mg).

Author (Country)	Dose (Daily, unless otherwise specified)
	Multi-nutrient
	A (2,666 IU, 89% RDA)
	D (400 IU, 50% RDA)
	C (120 mg, 133% RDA)
	E (60 mg, 400% RDA)
	B1 (1.2 mg, 100% RDA)
	B2 (1.4 mg, 108% RDA) B3 (14 mg, 88% RDA)
	B5 (14 mg, 88% KDA) B5 (5 mg, 100% AI)
	B6 (3.0 mg, 176% RDA)
	B7 (30 μg, 100% AI)
	Folic acid(600 µg, 150% RDA)
	B12 (200 µg, 8333% RDA)
	Ca (240 mg, 20% RDA)
	Cu (2000 µg, 222% RDA)
	Fe (12 mg, 150% RDA)
	I (150 μg, 100% RDA) Mg (100 mg, 24% RDA)
	Mg (100 mg, 24% RDA) Se (60 μg, 109% RDA)
Allsup et al., 2004 (UK) [REF]	Zn (14 mg, 127% RDA)
	Vitamin E (6.8 mg, 45% RDA)
	C (200 mg, 222% RDA)
	B1 (7.5 mg, 625% RDA)
	B2 (9 mg, 692% RDA)
	B3 (35 mg, 219% RDA)
	B5 (15 mg, 300% AI)
Asciutti-Moura et al., 1993 (France)	B6 (11 mg, 647% RDA)
	A (9900 IU, 330% RDA)
	D (400 IU, 50% RDA)
	E(12.2  mg, 123%  RDA)
	C (75 mg, 83% RDA) B1 (thiamine hydrochloride) (15 mg, 1250% RDA)
	B2 (10 mg, 769% RDA)
	B3 (Nicotinamide) (50 mg, 313% RDA)
	B5 (35 mg, 700% AI)
	B6 (25 mg, 1167% RDA)
	B7 (100 μg, 333% AI)
	Folate (200 µg, 50% RDA)
	B12 (25 μg, 1042% RDA)
	Ca (144 mg, 12% RDA)
	Fe (5 mg, 63% RDA)
	Mg (75 mg, 18% RDA)
	Mn (750 µg, 33% AI)
Crieger et al. 2000 (Australia)	K (1500 $\mu$ g, 32% AI) 7r (6 mg 55% (BDA)
Grieger et al., 2009 (Australia)	Zn (6 mg, 55% RDA) E (90 mg, 600% RDA) with 50% RDA of vitamins and minerals:
	A (1332 IU, 45% RDA), D (4000 IU (100 μg (per paper), 500% RDA)
	C (30 mg, 30% RDA)
	B1 (0.6 mg, 50% RDA)
	B2 (0.6 mg, 46% RDA)
	B3 (6.0 mg, 38% RDA)
	B6 (0.9 mg, 53% RDA)
	Folic acid (100 µg, 25% RDA)
	B12 (1 μg, 42% RDA)
	Cu (0.8 mg, 89% RDA)
Meydani et al., 2004 (US)	Fe (5 mg, 63% RDA)

	I (75 μg, 50% RDA)				
	Se (25 µg, 45% RDA)				
Zn (7 mg, 64% RDA)					
	Note: values taken for Meydani et al., 2007 pg 1168				
	A (3330 IU, 111% RDA)				
	E (15 mg, 100% RDA)				
Monget et al., 1996 (France)	C (120 mg, 133% RDA)				
	Zn (20 mg, 182% RDA)				
	Single Nutrient				
	8				
Favrat et al., 2011 (Switzerland)	B12 (1000 μg, 41667% RDA)				
Ter Riet et al., 1995 (The					
Netherlands)	C (1000 mg, 1111% RDA)				
Arcasoy et al., 2001 (Turkey)	Zinc (30 mg, 273% RDA)				

Author	Dose (Daily, unless otherwise specified)
	D (100 IU, 13% RDA)
Bonjour et al., 2011 (France)	Ca (302mg, 25% RDA)
	D (400 IU, 50% RDA)
Bonjour et al., 2013 (France)	Ca (800 mg, 67% RDA)
Mocanu et al., 2009 (Romania) *Used paper values - paper different from abstract for	D (5000 IU, 625% RDA)
25(OH)D	Ca (320 mg, 27% RDA)
Bonjour et al., 2009 (France)	D (100 IU, 13% RDA) Ca (302mg, 25% RDA)
	Ca (302mg, 23/0 KDA)

Authors	Dose (Daily, unless otherwise specified)
	C (31.5 mg, 35% RDA)
	B1 (0.44 mg, 37% RDA) B6 (0.81 mg, 48% RDA)
Van der Wielen et al., 1995 (The	Folic acid (63 µg, 16% RDA)
Netherlands)	B12 (1.10 μg, 46% RDA)
Bermejo et al., 2009 (Spain) Using Centre M	Folic acid (200 µg, 50% RDA)
and C data only	(food folate estimated to provide remaining 50% RDA)
	D (640 IU, 80% RDA)
	E (16 mg, 107% RDA)
	C (180 mg, 200% RDA)
	B1 (1.6 mg, 133% RDA)
	B2 (2.0 mg, 154% RDA)
	B3 (21 mg, 131% RDA)
	B5 (5 mg, 100% AI)
	B7 (30 μg, 100% AI)
	Folic acid (400 $\mu$ g, 100% RDA)
Adolphe et al., 2009 (Canada)	B12 (4 μg, 167% RDA)
Keane et al., 1998 (Ireland)	Folic acid (76 µg, 19% RDA)

Amount	Day 1	Amount	Day 2	Amount	Day 3	Amount	Day 4	Amount	Day 5
BREAKFAST	No Juice				Soy Beverage		Half amount of milk		Vegetarian (lacto-ovo)
250 ml	Milk, 2%	250 ml	Milk, 1%	250 ml	Soy beverage, enriched	125 ml	Milk, 1%	125 ml	Soy beverage, enriched
53 g	Egg, hard boiled	125 ml	Cranberry juice	14 g	Apricot (2 each)	125 ml	Grape Juice		
150 ml (30 ml)	Super Oatmeal (Almond Butter)	212 g	Basil, Oregano, Mushroom and Spinach quiche	125 g	Frittata	125 ml	Super oatmeal	125 ml (30 ml)	Super oatmeal (Almond butter)
70 g (15 ml)	Bread, WW [2sl] (Margarine)	35 g (23 ml)	Bread, WW [1 sl] (Almond Butter)	100 ml (30 ml)	Yogurt (Granola)	69 g	Kiwi (each)	60 g	Scrambled egg
				125 ml	Mashed sweet potato	80 g	Apple bacon mini loaf		
LUNCH									
125 ml	Milk, 2%	250ml	Milk, 1%	125 ml	Soy milk	250 ml	Milk, 1%	250 ml	Milk, 1%
125 ml (30 ml)	Endive and fennel salad (Italian dressing)	125 ml	Soybean (edamame)	180 ml	Creamed spinach	100 ml (15 ml)	Mashed carrots (Butter)	125 ml	Squash cubes
125 ml	Cream of mushroom soup (prep w milk)	125 ml	Tomato juice, Iow sodium	180 ml	Squash, carrot, ginger soup				
100 ml	Brown rice	125 g	Baked red potatoes	125 ml	Fried rice with carrots and peas	100 g	Baked potato	59 g 10 ml	French bread (1 sl) Butter + garlic
90 g	Meatloaf	90 g (15 ml)	Baked Salmon (Margarine)	120 g	Tandoori chicken	150 ml	Meat loaf	250 g	Vegetarian no- pasta Lasagna

 Table 13. Five-Day Super-Menu Sample Menu

90 ml	Rhubarb ckd w sugar			15 g	Oatmeal cookie (each)	100 g	Cinnamon pull- apart loaf	100 ml (40 ml)	Yogurt (Granola)
DINNER									
125 ml	Milk, 2%	125 ml	Milk, 1%	175 ml	Soy beverage, enriched	125 ml	Milk, 1%	125 ml	Soy beverage, enriched
180 ml	Broccoli, ckd	125 ml	Broccoli, ckd	125 ml	Kale and Red Cabbage Salad			250 ml	Arugula (125 ml), clementine (74g), cheese (20g) and pumpkin seeds (30ml)
100 ml	Brown Rice	125 ml (20 ml)	Baked mashed sweet potatoes (Margarine)	59 g	Sour dough bread	100 ml	Make ahead hash/mashed potatoes	130 ml	Brown Rice
125 g	Bok Choy mushroom and tofu soup					180 ml	Fish stew	180 ml	Cream of spinach soup
90 g (15 ml)	Multigrain Tilapia (Margarine)	150 g	Liver and onions	180 ml	Beef and vegetable stew	200 ml	Turkey quinoa chili	180 ml	Curry chickpea
100 ml (30 ml)	Yogurt (Super granola)	74 g	Clementine (each)	100 g	Applesauce Banana bread w choc chips	100 g	Pumpkin pie		

FOODS AND INGREDIENTS	CHOICES			
Vegetables and Fruit	Vegetables: Bell pepper (red), Broccoli, Cabbage (red), Carrot, Eggplant, Endive			
	(curly), Fennel, Kale, Mushrooms, Potatoes w skin, Spinach, Squash (butternut,			
	zucchini), Sweet potatoes			
	Fruits: Apricots, Clementine, Oranges			
Grain Products Bran, Brown Rice, Quinoa, Wheat germ				
Meat and Alternatives	Nut butters (almond butter)			
	Black beans, Chickpeas, White beans			
	Nuts/seeds: Almond, Flax, Pecan, Pumpkin, Squash, Sunflower, Walnut			
Milk and Alternatives	Cheese (Ricotta, Mozzarella, Swiss), Milk, Soy milk, Yogurt			
Fats and Oils	Butter, Canola oil, Margarine,			
Herbs and Spices	Herbs: Basil, Bay leaf, Cilantro, Coriander, Oregano, Parsley, Rosemary, Thyme			
-	Spices: Cinnamon, Chili/cayenne pepper, Cloves, Cumin, Garlic, Ginger (ground			
	vs root), Nutmeg, Paprika, Turmeric			

Table 14. Key foods used to meet DRIs in Super-menus

**Table 15.** Between-home comparison of planned menus and the Dietary Reference Intake for calories, protein and micronutrients

Nutrients Mean±SD [Median]	RDA/AI	Home A	Home B	Home C	Home D	Home E
Calories, kcal		2096 ± 324 <sup>ab</sup>	2008 ± 213 <sup>ab</sup>	1748 ± 253ª	$2022 \pm 265^{ab}$	2358 ± 349 <sup>b</sup>
Protein, g		88.6 ± 20.0 <sup>ab</sup>	86.2 ± 11.0 <sup>ab</sup>	$76.9 \pm 8.96^{ab}$	72.7 ± 13.7ª	95.2 ± 15.5 <sup>b</sup>
Dietary Fibre, g		$20.4 \pm 2.83^{a}$	18.4 ± 4.47 <sup>ab</sup>	15.8 ± 2.93 <sup>ab</sup>	$15.6 \pm 2.90^{b}$	20.1 ± 2.94 <sup>ab</sup>
Vitamin A, RAE	700F/900M	1038 ± 635 <sup>ab</sup> [828]	$903 \pm 248^{a}$	986 ± 689 <sup>ab</sup> [725]	1152 ± 716 <sup>ab</sup> [995]	1873 ± 75 <sup>b</sup> [1672]
Vitamin D, µg	20	6.78 ± 1.33 <sup>†a</sup>	$7.61 \pm 2.06^{\dagger a}$	8.79 ± 11.1 <sup>†a</sup> [4.98]	8.24 ± 1.03 <sup>†a</sup>	13.1 ± 0.53ª
Vitamin E, mg	15	5.27 ± 2.50 <sup>†a</sup> [4.39]	$3.85 \pm 1.96^{\dagger a}$	5.01 ± 1.73 <sup>†a</sup>	$5.52 \pm 0.96^{\dagger a}$	$5.98 \pm 0.52^{\dagger a}$
Vitamin C, mg	75F/90M	120.7 ± 27.8 <sup>ab</sup>	105.2 ± 38.0 <sup>ab</sup>	$88.9 \pm 24.6^{a}$	$103.9 \pm 21.4^{ab}$	126.9 ± 7.13 <sup>b</sup>
Thiamin, mg	1.1F/1.2M	1.16 ± 0.21ª	$1.46 \pm 0.32^{ab}$	1.44 ± 0.25 <sup>ab</sup>	$1.45 \pm 0.28^{ab}$	$1.64 \pm 0.27^{b}$
Riboflavin, mg	1.1F/1.3M	$2.07 \pm 0.40^{a}$	$3.08 \pm 0.36^{b}$	$2.37 \pm 0.16^{ac}$	$2.79 \pm 0.34^{bcd}$	$2.93 \pm 0.32^{bd}$

Niacin, NE	14F/16M	$26.7 \pm 6.23^{ab}$	23.3 ± 9.58ª [20.6]	$27.5 \pm 4.52^{ab}$	$20.1 \pm 6.72^{a}$	$33.7 \pm 5.04^{b}$
Pantothenic acid, mg	5 <sup>1</sup>	7.24 ± 0.86 <sup>a</sup>	8.05 ± 1.05 <sup>a</sup>	$6.72 \pm 0.76^{a}$	6.98 ± 1.37 <sup>a</sup>	12.32 ± 0.87 <sup>b</sup>
B6, mg	1.5F/1.7M	$1.33 \pm 0.4^{a}$	1.83 ± 0.50 <sup>a</sup>	$1.62 \pm 0.21^{a}$	$1.52 \pm 0.42^{a}$	$1.80 \pm 0.25^{a}$
Folate, µg DFE	400	294.3 ± 78.1 <sup>ab</sup>	189.8 ± 56.7 <sup>†a</sup>	271.2 ± 57.4 <sup>ab</sup>	2 <i>13.0 ±</i> 57.9ª [190.4]	336.2 ± 13.4 <sup>b</sup>
B12, μg	2.4	7.09 ± 8.76ª [4.34]	15.1 ± 1.03ª	$9.64 \pm 2.79^{a}$	15.2 ± 9.06ª [12.0]	9.78 ± 8.26ª [6.32]
Calcium, mg	1200	889 ± 165ª	1032 ± 159 <sup>a</sup>	962 ± 133ª	1387 ± 199 <sup>b</sup>	1506 ± 210 <sup>b</sup>
Copper, mg	0.9	1.43 ± 1.33 <sup>a</sup> [0.98]	$0.80 \pm 0.17^{a}$	$1.03 \pm 0.13^{a}$	1.48 ± 1.68ª [0.85]	1.78 ± 1.44ª [1.23]
lron, mg	8	14.6 ± 5.73ª [12.1]	10.6 ± 1.50 <sup>a</sup>	10.88 ± 1.79 <sup>a</sup>	$10.50 \pm 0.72^{a}$	12.6 ± 1.85ª
Magnesium, mg	320F/420M	234.7 ± 45.4ª	216.5 ± 33.3ª	269.2 ± 37.3*ab	232.4 ± 45.7ª	325.1 ± 49.1 <sup>b</sup>
Manganese, mg	1.8F/2.3M <sup>1</sup>	3.91 ± 0.97 <sup>a</sup>	2.40 ± 1.34 <sup>a</sup>	$3.34 \pm 0.74^{a}$	$2.96 \pm 0.82^{a}$	$3.90 \pm 1.25^{a}$
Phosphorus, mg	700	1123 ± 76.3ª	1299 ± 184 <sup>a</sup>	1363 ± 177 <sup>a</sup>	1276 ± 222 <sup>a</sup>	1742 ± 187 <sup>b</sup>
Potassium, mg	4700 <sup>1</sup>	2841 ± 564ª	2532 ± 404ª	2711 ± 388ª	2534 ± 429ª	3653 ± 411 <sup>b</sup>
Selenium, µg	55	81.3 ± 13.3ª	93.2 ± 16.7 <sup>ab</sup>	107.3 ± 13.9 <sup>ab</sup>	80.1 ± 11.6 <sup>a</sup>	111.5 ± 32.1 <sup>b</sup>
Sodium, mg	2300	4343 ± 3066 <sup>a</sup> [3219]	2958 ± 825 <sup>a</sup>	2426 ± 321ª	3277 ± 776 <sup>a</sup>	3333 ± 697ª
Zinc, mg	8M/11F	9.27 ± 2.20 <sup>ab</sup>	8.61 ± 1.71ª	8.50 ± 1.35 <sup>a</sup>	8.17 ± 1.40*a	12.25 ± 3.48 <sup>b</sup>

F=Female; M=Male; RDA = Recommended Dietary Allowance; SD = standard deviation; <sup>1</sup>Represents an AI rather than an RDA; Mean $\pm$ SD: † Represent values < 50% of RDA; *values between 50-75% of RDA in italics*; <sup>M</sup> = Males only; <sup>a,b,c,d,e</sup> Values with different superscripts indicate a significant difference at p<0.01; [Boxed] values represent the median, and indicate skewness in the data with a >10% difference between: ((mean-median)/mean)

RDA/AI	Home Average	Super Menu Average
	2046 ± 333	2074 ± 244
	83.9 ± 15.8	94.6 ± 9.57
	18.0 ± 3.72	23.4 ± 1.53*
700F/900M	1190 ± 695	2721 ± 1426
20	8.90 ± 5.29†	11.2 ± 2.54
15	5.13 ± 1.74†	12.6 ± 4.08*
75F/90M	109.1 ± 27.8	128.2 ± 44.9
1.1F/1.2M	$1.43 \pm 0.30$	1.59 ± 0.33
1.1F/1.3M	$2.65 \pm 0.49$	3.54 ± 1.33
14F/16M	$26.3 \pm 7.79$	36.8 ± 6.28*
5 <sup>1</sup>	8.26 ± 2.31	10.5 ± 3.03
1.5F/1.7M	$1.62 \pm 0.40$	2.29 ± 0.72
400	260.9 ± 89.5	509.3 ± 92.7*
2.4	11.4 ± 7.24	17.4 ± 19.6
1200	1155 ± 298	1621 ± 166*
0.9	1.31 ± 1.14 [0 99]	2.75 ± 2.45
8	$11.9 \pm 3.17$	15.3 ± 2.43*
320F/420M	255.6 ± 56.1 <sup>M</sup>	446.9 ± 39.3
1.8F/2.3M <sup>1</sup>	3.30 ± 1.15	4.69 ± 1.19
700	1361 ± 267	1733 ± 152*
4700 <sup>1</sup>	2854 ± 593	4018 ± 489*
55	94.7 ± 22.2	109.0 ± 12.1
2300	3267 ± 1547	2298 ± 385*
8M/11F	9.36 ± 2.54	12.5 ± 1.37*
	 700F/900M 20 15 75F/90M 1.1F/1.2M 1.1F/1.3M 14F/16M 5 <sup>1</sup> 1.5F/1.7M 400 2.4 1200 0.9 8 320F/420M 1.8F/2.3M <sup>1</sup> 700 4700 <sup>1</sup> 55 2300	2046 ± 333 $83.9 \pm 15.8$ $18.0 \pm 3.72$ 700F/900M $1190 \pm 695$ [979]20 $8.90 \pm 5.291$ [7.37]15 $5.13 \pm 1.741$ 75F/90M $109.1 \pm 27.8$ 1.1F/1.2M $1.43 \pm 0.30$ 1.1F/1.3M $2.65 \pm 0.49$ 14F/16M $26.3 \pm 7.79$ 51 $8.26 \pm 2.31$ 1.5F/1.7M $1.62 \pm 0.40$ 400 $260.9 \pm 89.5$ 2.4 $11.4 \pm 7.24$ [8.96] 12001200 $1.155 \pm 298$ 0.9 $1.31 \pm 1.14$ [0.99] $8$ 1.9 $\pm 3.17$ 320F/420M $255.6 \pm 56.1^{M}$ 700 $1361 \pm 267$ 47001 $2854 \pm 593$ 55 $94.7 \pm 22.2$ 2300 $3267 \pm 1547$

Table 16. Comparison of planned menu and super menu averages to Dietary Reference Intakes for calories, protein, fibre, and micronutrients

F=Female; M=Male; RDA = Recommended Dietary Allowance; SD = standard deviation <sup>1</sup>Represents an AI rather than an RDA; Mean±SD: † Represent values < 50% of RDA; *values between 50-75% of RDA in italics*; <sup>M</sup> = Males only; [Boxed] values represent the median, and indicate skewness in the data with a >10% difference between: ((mean-median)/mean); \*p<0.05 (Two-tailed t-test between Home Menus (n=35) and Super Menus (n=5), assuming unequal variance); Note: Assumption of variance may not have been met in the t-test by comparing 35 Home Menu days with 5 Super-Menu days.

IN-PERSON RESIDENT/FAMILY FOCUS GROUPS	Ν	%
GENDER	71	
Women	53	75
Men	18	25
ROLE	71	
Resident	45	63
Family	17	24
Staff	9	13
KEY INFORMANT INTERVIEWS	Ν	Percentages
GENDER	10	
Women	9	90
Men	1	10
ROLE	10	
Industry	2	20
Clinical Practice	4	40
Others (*MOHLTC officer, Culinary expert, Consulting	4	40
RD firm president, Corporate LTC Menu Planner)		
WEBINARS†	Ν	Percentages
LOCATION	45	
Alberta	9	20
British Columbia	3	7
Manitoba	1	2
Nova Scotia	2	4
Ontario	23	50
Prince Edward Island	2	4
Saskatchewan	5	11
OCCUPATION	45	
Registered Dietitian	29	63
Nutrition Manager	11	24
Chef	1	2
	4	9
Others (Food supervisor, program lead, CQI Coordinator, Dietitian in Education)		
Dietitian in Education)	45	
Dietitian in Education)         YEARS OF WORK	<b>45</b> 5	11
Dietitian in Education)         YEARS OF WORK         < 1 year		
Dietitian in Education)         YEARS OF WORK         < 1 year	5 9	20
Dietitian in Education)         YEARS OF WORK         < 1 year	5	

## Table 17. Participant characteristics

† Note: All webinar respondents were female; 3 dietitians-only groups, 8 mixed staff groups

	uotes on the Acceptability of Food Fortification in Long-Term Care
Participant	Direct quotes
	Reflections on Current Strategies
Registered Dietitian (RD)16	{When asked about considering micronutrients when thinking about malnutrition in residents}*We focus on <i>macronutrients</i> , because they're the things we can do the most with.
RD17	If we focus on good, nutrient-dense foods that are high in the macronutrients – I'm hopeful that we get the micronutrients.
Key Informant (KI)4, Corporate LTC Menu Planner	{When asked about concerns with poor intake of residents} [It's] quite a lot of food We know the residents can't eat all the food, but we have to provide it because that's a Ministry license [requirement]
KI7, Ministry of Health and Long-Term Care officer	The residents wanted to know whether they can actually ask for smaller portions at the point of service or even as part of the menu planning, they had concerns with following Canada's Food Guide, saying that it was too much volume or too much weightThe intent was not to require that the homes adhere strictly to the portion sizes and numbers of servings as per Canada's Food Guide[but to focus on] the variety aspect and fresh fruits and vegetables.
Nutrition Manager (NM)36	{On food vs. pills and movement in LTC to reduce polypharmacy} Giving another pill isalmost the straw to break the camel's back If it's in the food, then maybe we can eliminate some of those medications.
NM36	{On side effects of Oral Nutritional Supplements (ONS)} The reality is, we <i>do</i> have supplements The difficulty is that when they drink one of those tetras [ONS]they're full! So they're not getting fibre or other things that they needthen you're ending up having to look at bowel protocols at the other end.
KI2, Health and Marketing Specialist for Food Supplier	{On redundancy of current strategies} We have the powders, the formulas, whatever, but it doesn't seem to be getting anywhereOur residents have to show malnutritionto actually get the referral to the RD [registered dietitian], for the RD to see them and give them the supplement. So if we try to meet those needs before that happens to be <i>pro</i> active [emphasis noted in recording] instead of <i>reactive</i> , I think it would be a good idea.
Family Resident Council (FRC)2	{On preference for current strategy of pill supplementation} At least if vitamins are being administered separately, it would ensure adequate amounts of vitamins are being consumed.
· · · ·	Appropriateness of Fortification Strategy
KI1, Industry Brand Manager	{On concerns with a fortification strategy} Once you take the product and add micronutrientsautomatically, you'll increase the cost.
KI5, Culinary Expert	If you think about somebody unwrapping a bouillon cube or a packet [to add fortificant formulation]Someone is going to throw the thing in with the packet still on [and] you don't know what they dilute with!There's just too many variables [for adding fortificant formulation to current food products]
NM36	{When adding fortificant formulation to a food product in-house, concern about accuracy} A scoop – is it a full scoop, or is it over-the-top scoop, or is it not quite up to the level scoop?
RD9	{On whether the strategy is food or medication} Safety issues[and the] legal ramifications[of] asking a health careor food service aideand making them responsible for a vitamin, which is bordering on a medication.
Resident Council (RC)1	If taste was taken away, then it's useless.
Family council (FC)2	{On uncertainty of adequacy of food fortification strategy} Those residents who are most likely to suffer from nutrient deficiency are those with decreased appetite. If [residents] are not consuming sufficient amounts of food, nutrient enhancement of food would be of little or no benefit to these residents.
	Promoting feasibility of a fortification strategy
RD28	{On need to make fortification easy to incorporate into daily routine} [Make it] part of a recipe [where] it has been tasted and everything has been worked out There has to be good tracking system to make sure that what is supposed to be received isdelivered and monitoredIf we don't consume all of it, at least have an idea of that

 Table 18.

 Exemplar Ouotes on the Acceptability of Food Fortification in Long-Term Care

KI7 - Ministry of Health	The assessment part of itWho would be the candidate for the supplementation Across
and Long-Term Care	the board, how would that process work? What directions would we give?
officer	
	{On need for multi-level involvement} If they understand why it needs to be done, the
NM5	reasons for it and the importance of it, it seems to happen better – on a more consistent
	basis, and they feel better informed, know that what they're doing is, in actuality, better for
	the resident that they're feeding. They get the ownership of doing the thing correctly.
	Determining the potential effectiveness of a fortification strategy
	{On need to elaborate on strategy before effectiveness can be appropriately determined}A
NM36	lot of residents request small portions. And if I know there are more nutrients in the
	products, then even that small portion will help them. So I do see that as a positive. The
	difficulty is, how do we get it into that product?
	{On need to demonstrate cost-benefit of strategy} It's this notion of cost-benefit as
KI1 – Food Industry	wellwhatever it may costSomething as simple as this, how can it save the facility
Expert	money over the long-run, in terms of treatment of people in frail situations [or] quality of
	life in general.
564	Who, when, why, how? Many variables and many decisions to be considered regarding who
FC4	would administer, who would monitor it [in-house fortification] and to have it administered?
	Quality of lifeGood food is an asset but not necessarily should we be prolonging life [for
	all residents].
	Overall acceptance of a fortification strategy
EGA	Family members appreciated that the strategy "offers an extra choice for residents and
FC4	families to assist in maintaining better health"
ED CO	[Food fortification is an] interesting approach to adding nutrients towhat is missing in a
FRC2	fuller meal.
	[Residents are] not eating a lot to begin with, so if we would be able to have some fortified
NM3	food that we are able to give them, in small amounts, to reintroduce them to eating, I think
	that would be very beneficial.
ND (26	A lot of residents request small portions. And if I know [that if] there are more nutrients in
NM36	the products, then even that small portion will help them.

\* {Braces} provide additional context for quotes

FOOD VEHICLES	SPECIFIC REASONS			
BREAKFAST FOOD	Well-consumed; Best meal of the day			
Hot cereal (oatmeal, cream of	Appropriate for different texture needs			
wheat)				
FLUIDS				
Broth	• Used as-is, or to make 'from scratch' soup, or in stocks/sauces			
Soup	• Comfort food; eaten even when have no appetite for dinner			
	• Available at multiple meals (lunch and dinner)			
Juice	Contains nutrients on its own			
	Residents may prefer this to milk			
Milk	Common additive to foods			
	• Can have on own or incorporate into other foods			
Coffee	Well-consumed			
	• Available throughout the day (most meals/snacks)			
SIDE				
Mashed Potatoes	Appropriate for different texture needs			
	Accompanies different sides			
DESSERT	Well-consumed; large variety is provided			
Pudding	Appropriate for different texture needs			
Ice-Cream	Well-liked; even by different cultures			
	Contains nutrients on its own			
(canned, pureed)				
(canned, pureed)	Appropriate for different texture needs			
CONDIMENTS/ GARNISH/ TOPPING	Pre-measured; Versatile; Small amount; maximize consumption opportunities			
	Easy to transport			
	Can go in soup/stock/sauces			
Whipped topping	Versatile; Goes on/in various desserts			
Coffee creamer	Coffee is well-consumed (staple beverage)			
Jam/Jelly	Can go on toast or pastries (variety)			

# Table 19. Potential Food Vehicles for Micronutrient Food Fortification in Long-Term CareFOOD VEHICLESSPECIFIC REASONS

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