Diet and frailty in Norwegian older adults

The Tromsø Study

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‘Until the moment it is upon us, old age is something that only affects other people.’

Simone de Beauvoir, 1970

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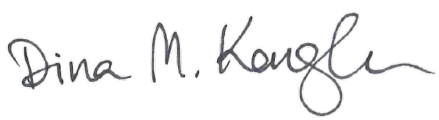
Oslo, April 2024



Dina Moxness Konglevoll

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SUMMARY

Background: With a rapidly ageing population, age-related syndromes like the frailty syndrome is rising both nationally and globally. Frailty is characterized by increased vulnerability and reduced resilience to stressors in older adults. Frail and pre-frail individuals have higher risk of ill health and need for health care services. Diet is an important modifiable risk factor for the frailty syndrome. Protein, fish, and an overall healthy diet have been independently associated with frailty; however, the effect of long-term intake remains unknown and the results are inconsistent. Increased knowledge about the association between diet and frailty may contribute to future enhanced prevention, management and, on an individual level, even reversal of the frailty syndrome. This will promote healthier ageing in the population, which has substantial economic and societal benefits.

Aims: The aim of this PhD thesis was to elucidate the longitudinal association between diet and frailty in Norwegian older adults. Specifically, we aimed to analyse the relationship between previous intake of daily protein and frequency of lean, fatty and total fish on later pre-frailty/frailty, and also the association between long-term patterns of intake of protein, fish and the overall diet over 21 years, and pre-frailty/frailty in older age.

Methods: This thesis used data from the last four surveys of the population-based Tromsø Study: Tromsø4 (baseline, 1994–95) to Tromsø7 (follow-up, 2015–16). The study population consisted of men and women (Paper I, n = 3726, Paper II, n = 4350, Paper III, n =715) who were aged ≥ 44 years at baseline (corresponding to ≥ 65 years at follow-up), with data on relevant dietary variables and frailty at follow-up. In Papers I and II, physical frailty at follow-up was defined by a modified version of Fried et al.'s definition, by unintentional weight loss, exhaustion, low physical activity, low grip strength and slow walking speed, categorizing participants as 'frail' (≥ 3 characteristics present), 'pre-frail' (1–2 characteristics present), and 'robust' (none present). In Paper III, frailty was defined using a 41-item frailty index, assessed as a continuous scale between 0–1 with higher scores indicating more severe frailty. In Paper I, the exposure was daily protein intake (in g/kg bodyweight and g/megajoule (MJ)) in Tromsø4 and Tromsø7, and patterns of protein intake over 21 years (i.e. between Tromsø4 and Tromsø7), and the outcome was pre-frailty/frailty. In Paper II, the exposure was low frequency (0–3/month), medium (1–3/week) and high (≥ 4 times/week) of lean, fatty, and total fish intake in Tromsø6 (2007–08), and stable patterns of total fish intake over 21 years. The outcome was pre-frailty. The patterns of protein and fish intake in Papers I and II were

constructed via cross-tabulation. In Paper III, the exposure was five dietary trajectories over 21 years based on three diet scores measured in Tromsø4, Tromsø5 (2001) and Tromsø7, and the outcome was the frailty index score. The diet scores assessed the diet according to the Nordic Nutrition Recommendations (NNR) 2023. The dietary trajectories were created using group-based trajectory modelling. The diet–frailty associations were analysed using multivariable logistic (Papers I and II) and linear (Paper III) regression, adjusted for confounding baseline variables.

Results: In Paper I, the prevalence of pre-frailty and frailty at follow-up was 27% and 1%, respectively. A higher daily intake of protein in g/kg bodyweight was associated 57% lower odds of pre-frailty/frailty 21 years later (odds ratio (OR) = 0.43, 95% confidence interval (95% CI) = 0.31, 0.58). The patterns 'stable low' (OR = 1.90, 95% CI = 1.16, 3.09) and 'decreased' (OR = 1.85, 95% CI = 1.14,2.99) protein intake in g/kg bodyweight over 21 years were associated with 90% and 85% increased odds of pre-frailty/frailty, respectively, compared with a stable high pattern of intake. No associations were found between protein in g/MJ and pre-frailty/frailty. In Paper II, the prevalence of pre-frailty was 28%. A high intake of lean, fatty, and total fish were associated with 28% (OR = 0.72, 95% CI = 0.53,0.97), 37% (OR = 0.63, 95% CI = 0.44,0.92) and 31% (OR = 0.69, 95% CI = 0.52,0.91) lower odds of pre-frailty 8 years later, compared with a low intake, respectively. For fatty fish, a medium intake was associated with 19% lower odds of pre-frailty (OR = 0.81, 95% CI = 0.68,0.97). A stable high total fish intake over 21 years was associated with lower odds of pre-frailty compared with a stable low intake (OR = 0.59, 95% CI = 0.38,0.91). In Paper III, five dietary trajectories over 21 years were identified. The trajectories 'moderately healthy' and 'healthy increase' were associated with 0.02 (β = –0.02, 95% CI = –0.04, –0.002) and 0.03 (β = –0.03, 95% CI = –0.06, –0.007) lower frailty index score in Tromsø7, respectively, compared with the 'unhealthy' trajectory.

Conclusion: This thesis consistently demonstrated that diet in mid-life influences frailty in older age. Our findings suggest that a higher protein intake, frequent intake of lean, fatty, and total fish, and an overall healthy diet in line with the NNR2023 may be associated with lower pre-frailty and frailty risk in older age. Specifically, our studies emphasize the importance of maintaining consistent healthy dietary habits through adulthood and into older age, as this was associated with lower frailty risk. This supports the promotion of a healthy lifestyle and diet, including adhering to dietary guidelines from adulthood mid-life, if not earlier, to facilitate

healthier ageing in the Norwegian population. However, more research is needed to confirm the association between long-term diet and pre-frailty and frailty.

SAMMENDRAG

Bakgrunn: Med en raskt aldrende befolking, øker forekomsten av aldersrelaterte tilstander som skrøpelighet både nasjonalt og globalt. Skrøpelighet er en sammensatt tilstand karakterisert av økt sårbarhet og redusert toleranse for stress og påkjenninger hos eldre. Skrøpelige og pre-skrøpelige individer har økt risiko for dårlig helse og økt bruk av helsetjenester. Kosthold er en viktig modifiserbar risikofaktor for skrøpelighet. Protein, fisk og et generelt sett sunt kosthold har blitt assosiert med skrøpelighet, men effekten av inntak over tid er ikke fastslått og resultatene er inkonsekvente. Økt kunnskap om sammenhengen mellom kosthold og skrøpelighet kan bidra til bedre forebygging, behandling og – på individnivå – til og med reversering av skrøpelighet. Dette vil fremme sunnere aldring i befolkningen, med potensielt betydelige økonomiske og samfunnsmessige fordeler.

Mål: Målet med denne doktorgradsavhandlingen var å belyse den longitudinelle sammenhengen mellom kosthold og skrøpelighet hos norske, eldre individer. Spesifikt ville vi undersøke sammenhengen mellom tidligere inntak av daglig protein, og hyppighet av mager, fet og total fiske og senere skrøpelighet/pre-skrøpelighet, samt sammenhengen mellom mønstre av inntak av protein, fisk, og hele kostholdet over 21 år, og pre-skrøpelighet/skrøpelighet blant eldre.

Metoder: Denne avhandlingen har brukt data fra de fire siste studiene i den befolkningsbaserte Tromsøundersøkelsen: fra Tromsø4 (baseline, 1994–95) til Tromsø7 (oppfølging, 2015–16). Studieutvalget bestod av menn og kvinner (Artikkel I, n = 3726, Artikkel II, n = 4350, Artikkel III, n = 715) som var ≥ 44 år ved baseline (tilsvarende ≥ 65 år ved oppfølging) og hadde data på relevante kostholdsvariabler, og skrøpelighet ved oppfølging. I Artikkel I og II ble fysisk skrøpelighet definert med en modifisert versjon av Fried's skrøpelighetsdefinisjon, basert på utilsiktet vekttap, utmattelse, lav fysisk aktivitet, lav gripestyrke og langsom ganghastighet. Deltagerne ble klassifisert som skrøpelige (≥ 3 karakteristikker til stede), pre-skrøpelige (1–2 karakteristikker) og robust (ingen karakteristikker). I Artikkel III ble skrøpelighet definert med en skrøpelighetsindeks basert på 41 helsevariabler, undersøkt som en kontinuerlig skala mellom 0–1 der høyere score indikerer mer skrøpelighet. I Artikkel I var eksponeringen daglig proteininntak (i g/kg kroppsvekt og g/kg megajoule (MJ)) i Tromsø4 og Tromsø7, og mønstre av proteininntak over 21 år (det vil si fra Tromsø4 til Tromsø7), og utfallet var pre-skrøpelighet/skrøpelighet kombinert. I

Artikkel II var eksponeringen lav (0–3 ganger månedlig), middels (1–3 ganger ukentlig) og høy (≥ 4 ganger ukentlig) hyppighet av inntak av mager, fet, og total fisk i Tromsø6 (2007–08), og stabile mønstre av fiskeinntak over 21 år. Utfallet var pre-skrøpelighet. Mønstrene av protein og fiskeinntak i Artikkel I og II ble identifisert ved krysstabulering. I Artikkel III var eksponeringen fem kostholdsmønstre basert på tre kostscorer målt i Tromsø4, Tromsø5 (2001) og Tromsø7, og utfallet var skrøpelighetsindeksen. Kostscorene målte deltagernes kosthold opp mot de nye nordiske kostrådene (NNR) 2023. Kostholdsmønstrene ble identifisert ved hjelp av group-based trajectory modelling. Assosiasjoner mellom kostholdsfaktorene og pre-skrøpelighet ble analysert ved multivariabel logistisk (Artikkel I og II) og lineær (Artikkel III) regresjon, justert for konfunderende baselinevariabler.

Resultater: I Artikkel I var forekomsten av pre-skrøpelighet og skrøpelighet ved oppfølging på henholdsvis 27% og 1%. Et økt daglig inntak av protein i g/kg kroppsvekt var assosiert med 57% lavere odds for pre-skrøpelighet/skrøpelighet 21 år senere (odds ratio (OR) = 0.43, 95% konfidensintervall (KI) = 0.31,0.58). Mønstrene stabilt lavt (OR = 1.90, 95% KI = 1.16,3.09) og synkende (OR = 1.85, 95% KI = 1.14,2.99) proteininntak i g/kg kroppsvekt over 21 år var assosiert med henholdsvis 90% og 85% høyere odds for pre-skrøpelighet/skrøpelighet sammenliknet med et stabilt høyt inntak. Ingen sammenheng ble observert mellom proteininntak i g/MJ og pre-skrøpelighet/skrøpelighet. I Artikkel II var 28% av deltagerne pre-skrøpelige. Et høyt inntak av mager, fet og total fisk var assosiert med henholdsvis 28% (OR = 0.72, 95% KI = 0.53,0.97), 37% (OR = 0.63, 95% KI = 0.44,0.92) og 31% (OR = 0.69, 95% KI = 0.52,0.91) lavere odds for pre-skrøpelighet 8 år senere, sammenliknet med et lavt inntak. For fet fisk var også et middels hyppig inntak assosiert med lavere odds (19%) for pre-skrøpelighet sammenliknet med et lavt inntak (OR = 0.81, 95% CI = 0.68,0.97). Et stabilt høyt totalt fiskeinntak over 21 år var assosiert med 41% lavere odds for pre-skrøpelighet sammenliknet med et stabilt lavt inntak. I Artikkel III identifiserte vi fem kostholdsmønstre over 21 år. Mønstrene 'moderat sunt' og 'sunt og økende' var assosiert med 0.02 og 0.03 lavere skrøpelighetsindeks score i Tromsø7, sammenliknet med et 'usunt' mønster.

Konklusjon: Denne doktorgradsavhandlingen har konsekvent vist at kosthold i voksen alder påvirker skrøpelighet i eldre alder. Våre funn tyder på at et høyere proteininntak, hyppig inntak av mager, fet og total fisk, samt et generelt sunt kosthold i tråd med NNR2023, kan være assosiert med lavere risiko for pre-skrøpelighet og skrøpelighet i eldre alder. Spesielt demonstrerer våre funn viktigheten av å opprettholde konsekvente sunne kostholdsvaner over

tid, da dette var gjennomgående assosiert med lavere risiko for skrøpelighet. Dette støtter arbeid som fremmer en sunn livsstil og et sunt kosthold, hos voksne, for å legge til rette for en sunnere aldring i den norske befolkningen. Mer forskning er imidlertid nødvendig for å bekrefte sammenhengen mellom langsiktig kosthold og pre-skrøpelighet og skrøpelighet.

LIST OF PAPERS

Paper I. **Konglevoll DM**, Hjartåker A, Hopstock LA, Strand BH, Thoresen M, Andersen LF, Carlsen MH. *Protein Intake and Risk of Pre-Frailty and Frailty in Norwegian Older Adults. The Tromsø Study 1994–2016*. J Frailty Aging. 11, 256–66 (2022).

Paper II. **Konglevoll DM**, Andersen LF, Hopstock LA, Strand BH, Thoresen M, Totland TH, Hjartåker A, Carlsen MH. *Fish intake and pre-frailty in Norwegian older adults. A prospective cohort study: the Tromsø Study 1994–2016*. BMC Geriatr. 23, 411 (2023).

Paper III. **Konglevoll DM**, Andersen LF, Thoresen M, Totland TH, Hopstock LA, Hjartåker A, Carlsen MH. *Dietary trajectories over 21 years and frailty in Norwegian older adults: the Tromsø Study 1994–2016.* Submitted to Eur J Nutr, December 2023.

ABBREVIATIONS

AHEI	Alternative Healthy Eating Index
BMI	body mass index (kg/m^2)
CI	confidence interval
DASH	Dietary Approaches to Stop Hypertension
DHA	docosahexaenoic acid
EPA	eicosapentaenoic acid
E%	proportion of total energy intake from protein
FFQ	food frequency questionnaire
GBTM	group-based trajectory models
HUNT	Trøndelag Health Study
IPW	inverse probability weighting
KBS	Kostberegningssystem
KI	konfidensintervall
LCn-3FA	long-chain omega-3 fatty acids
MAR	missing at random
MI	multiple imputation
MJ	megajoule
MDS	Mediterranean Diet Score
MMSE	Mini-Mental State Examination
NDG	Norwegian Dietary Guidelines
NOK	Norwegian krone
NNR	Nordic Nutrition Recommendations
RCT	randomized controlled trial
SPPB	Short Physical Performance Battery
SD	standard deviation
OR	odds ratio
Q1–Q5	quintiles 1–5 of diet scores
UiO	University of Oslo
WHO	World Health Organization

TABLES AND FIGURES

1 Introduction

1.1 Ageing

1.1.1 Health and life expectancy through history

In the pre-modern era, global life expectancy was approximately 30 years. Infectious diseases were widespread and child mortality high – as late as the year 1800, more than one-third of children died before the age of 5 and a higher proportion during adolescence (1). Only a small proportion of people lived longer lives and got old. From the nineteenth century, modernization and industrialization of society led to immense progress in public health, substantially increasing life expectancy in the countries that underwent early industrialization (1, 2). Over the last two centuries, there has been a shift from child mortality caused by acute diseases to adult mortality from chronic and degenerative diseases (2).

Between 1800 and 2019, global life expectancy more than doubled, from 29 years to 73 years and, in Europe, it increased from 33 years to 79 years (**Figure 1**). Similarly, Norwegian life expectancy increased from 48 years to 83 years between 1846 and 2019 (1).

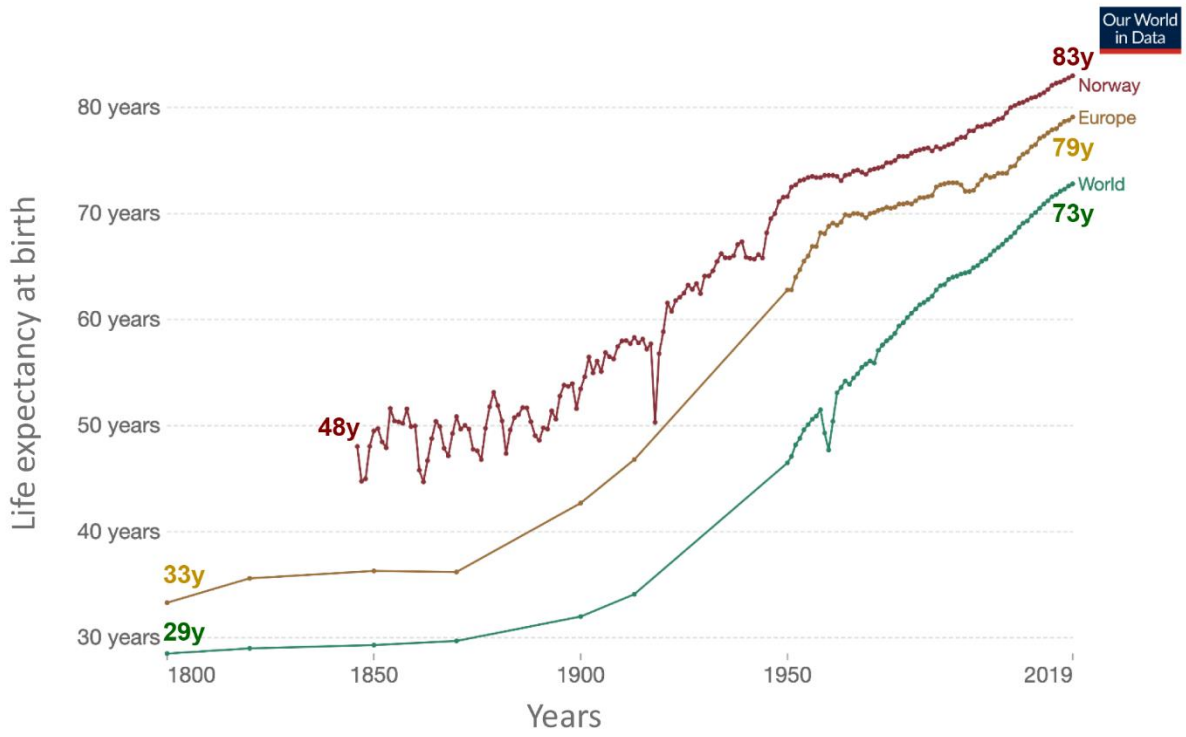

Figure 1 Human life expectancy 1800–2019: worldwide, Europe, Norway. y, years. Figure adapted from Roser, Ortiz-Ospina and Ritchie (1), data freely available for reproduction.

This increase in life expectancy is the crowning achievement for humanity of the modern age and reflects sustained improvements in health and healthcare, economic growth and social policy (1, 3, 4). Across the globe, women outlive men – as they have done since the early twentieth century (3). Also, in Norway, women live the longest: in 2017 the average life expectancy was 84 years for women and 81 years for men (4).

1.1.2 The ageing population

In addition to the increased life expectancy, the population – as a whole – is ageing. The share and number of older people in the world are growing rapidly (5), further exacerbated by reduced fertility rates (6). In fact, the population aged ≥ 60 years is growing at a faster rate than the total population in nearly all world regions (7). Globally, there were 703 million people aged ≥ 65 years in 2019. By 2050, that number is projected to have more than doubled, to 1.5 billion (8). This translates into an expected increase in the proportion of older adults (≥ 65 years) from about 9% in 2019 to 16% in 2050 (8). A similar demographic change is happening in Norway, where the proportion of people aged ≥ 65 years is expected to increase from 18% in 2020 to 27% in 2050 (9) **(Figure 2)**.

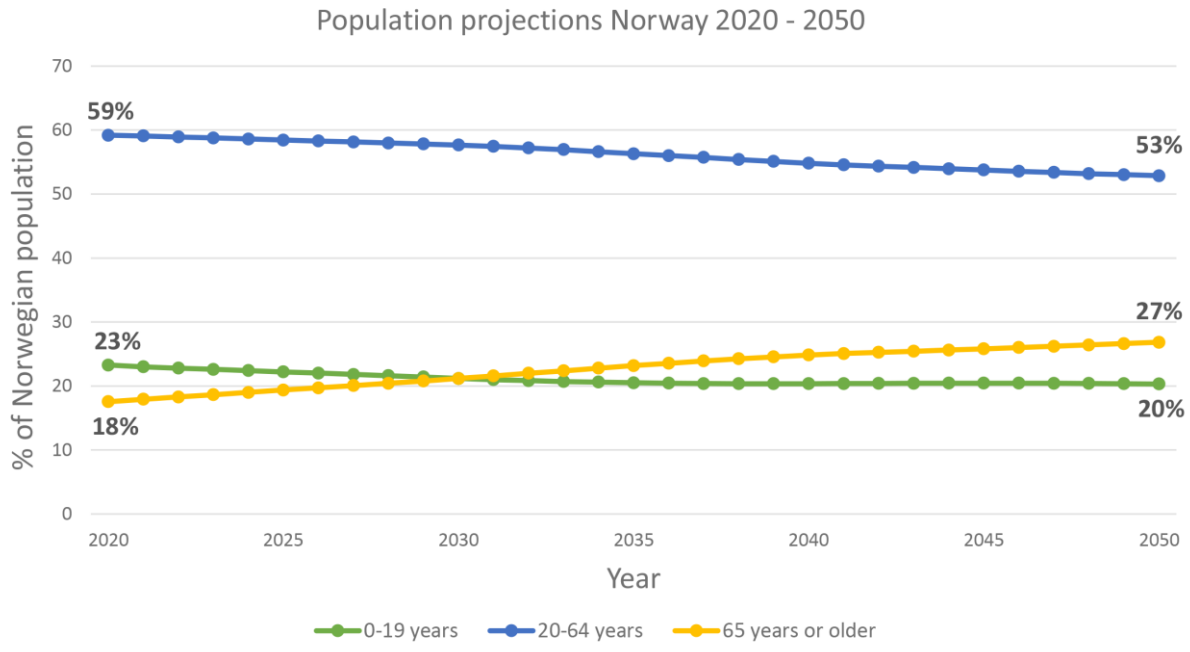

Figure 2 Population projections in Norway, 2020–2050, by age group: 0–19 years, 20–64 years (blue) and ≥ 65 years (yellow). The figures are based on data from Statistics Bank, Statistics Norway (9), and reproduced with permission from Statistics Norway.

Total life expectancy comprises both 'healthy life expectancy' (also known as 'healthspan',

i.e. period free from disease) and ‘years lived with disability’ (1, 2). In most countries, there has been an increase in both, but, overall, the increase in ‘years lived with disability’ has been slower than the increase in healthy years (1). Inhabitants in countries with higher healthcare expenditure and more accessible healthcare services, such as Norway and other high-income countries, tend to live more years disabilities compared with countries with lower healthcare expenditure (1).

1.1.3 Definitions of ageing

Ageing is one of the most complex and comprehensive processes in human life, and therefore not easily measured or defined. To date, there is not one universally accepted definition of the process of ageing, or of when a person is ‘old’ or what a typical ‘older person’ is (10). What it means to grow older has also been conditioned very much culturally and socially, and the role and status of older adults in society vary (11). Biologically, ageing can be viewed as the result of the gradual accumulation of molecular and cellular damage over the course of a lifetime (12). With time, this causes a decrease in physical and mental capacity, increased risk of disease, and ultimately, death. Beyond biological and genetic influences, the course of ageing is determined by people’s physical and social environments (e.g. their homes, neighbourhoods and communities), interconnected with their personal characteristics (e.g. sex, ethnicity and socioeconomic status) (11, 13). The ageing process progresses neither linearly nor consistently and is only loosely linked to chronological age (10, 13). Some 90 year olds remain active and enjoy good physical and mental functioning, whereas others may lose their good health and vitality in their 60s (13). Nevertheless, the ageing process is generally so pronounced from about 60–70 years of age, around retirement age in modern societies, that this is typically used as a cut-off for when individuals are considered to be old (7, 13, 14). In this thesis, ‘older adults’ are defined as those aged ≥ 65 years, if not specified otherwise.

1.1.4 Costs of ageing

Longer human lives may represent a valuable resource, because older adults possess unique life experiences and qualities that, if utilized, may benefit society and young people (15). However, the ability of older adults to actively contribute to society depends on their health and functionality.

The risk of chronic diseases, hospitalization and disability increases with age (13, 16), which is reflected in the gradual increased use of healthcare services with age (17). Older adults are more frequently admitted to, and stay longer in hospitals than younger patients (18). In 2011,

every third Norwegian krone (NOK) spent in the hospital setting was spent on older adults (18). Traditionally it was the family and relatives who took care of older adults, whereas today this responsibility lies with the public, the municipality and the state (18, 19). In 2011, two out of three NOK in the municipal nursing and care services went to the care of older patients (18).

Considering this, an ageing population is often perceived negatively from an economic point of view (20). Geriatric patients are typically more complex than younger patients, and more likely to suffer from multimorbidity. Common disorders and complaints in older adults include osteoporosis, falls and fractures, chronic pain, cognitive impairment and dementia, depression and loneliness, impaired vision and hearing, cancer, diabetes, and cardiovascular and lung disorders (18, 21). Multimorbidity is associated with more frequent use of healthcare services, higher healthcare costs, and increased use of medication (13, 22) (13). Polypharmacy (using five or more drugs on a daily basis) increases the risk of reduced effect or unwanted side effects of the prescribed drugs (22). In 2016, 67% of community-dwelling older adults in Norway used five or more prescribed drugs and 28% used ten or more drugs (21).

Poor health among older adults increases societal health expenditure, so it is in societies' best interest to invest in increasing the number of healthy life-years in older adults (20, 23), in line with the saying 'Add life to years, not years to life'. Prolonging the onset of the first chronic illness, i.e. prolonging one's healthspan closer to death, would squeeze total lifetime morbidity into a shorter span, thereby reducing the burden of disease (2, 24). If the health of older adults were to improve, the societal economic burden of an ageing population could decrease substantially, and in particular if the population's working life is extended (25, 26). Put simply: it is cheaper to prevent than to treat unhealthy ageing.

1.1.5 Healthy ageing

The United Nations declared the decade 2020–2030 as the 'Decade of Healthy Ageing' (27) to raise awareness on how societies may counteract increased healthcare costs and promote benefits by keeping older people healthy for as long as possible. However, healthy ageing is not merely the absence of disease in old age, but includes life satisfaction, well-being and maintenance of physical and cognitive function. In 2015, the World Health Organization (WHO) defined healthy ageing as 'the ongoing process of developing and maintaining the functional ability that enables wellbeing in older age' (13). Functional ability includes a

person's ability to meet their basic needs, grow, develop and make decisions, and covers the possibility of moving freely, building or maintaining relationships and, with this, participating and contributing to society (13).

Whether or not individuals will age in good health largely depends on what prerequisites they have had to make healthy and preventive choices throughout life, and there are large discrepancies in health and well-being in the older population (28). International and national studies show that more highly educated older adults have better health, functional capacity (29), and life expectancy (30, 31) than those with lower levels of education. Work towards healthy ageing must therefore include work to reduce social inequality (13). The best way forward to healthy ageing is not represented by disease treatments, but through the adoption of lifestyles that can prevent their onset (28).

Healthy ageing in Norway

The older population in Norway today is a heterogeneous group of individuals who have grown up with increasing wealth and increased life expectancy compared with previous generations (18). Results from the Trøndelag Health Study (HUNT) suggest that the increase in life expectancy in Norwegian older adults consists mostly of healthy years (32). The study showed that over the period 1995–2017, the expected healthspan after age 70 increased by an average of about 4 years, whereas the number of years lived with disability decreased **(Figure 3).** This is supported by projections from the WHO and the Norwegian Institute of Public over the previous two decades, suggesting that most of the increase in life expectancy was healthy years (33, 34). In line with this, emerging findings from Norwegian population-based studies report improvements in functionality (32), strength (35), hearing (36) and cognitive health (37) among today's older adults compared with previous generations. Thus, it appears that, despite living longer with chronic diseases (21), the Norwegian older population is, overall, healthier than before.

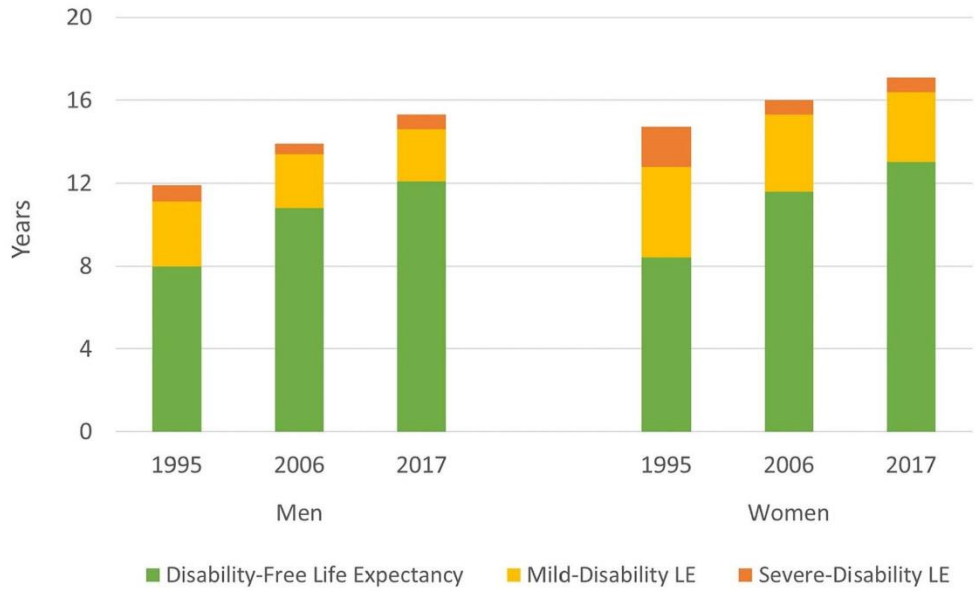

Figure 3. Life expectancy and years with/without disability at age 70 years in 1995, 2006 and 2017 for Norwegian men and women: years without disability (green), and years with mild (yellow) and severe (orange) disability. The figure is based on HUNT data, published in Storeng et al. (32). Reproduced with permission from authors and SAGE Publications.

Unfortunately, not all older adults experience healthy ageing, but many become frail.

1.2 Frailty

In many ways, frailty can be viewed as the opposite of healthy ageing. It is not a natural consequence of ageing but represents a dynamic phase between healthy ageing and disability. Although recognized as a clinical syndrome, frailty is not a medical diagnosis because it can have multiple underlying causes and thus manifests and progresses in a highly individual manner (38-40). Frailty is a complex syndrome resulting from multisystem loss of functional reserves, which, over time, makes individuals less resilient to stressors such as infection, medication change, falls or a change in living situation (40). Frail people are at higher risk of adverse health outcomes such as falls, diseases, reduced quality of life, hospitalization rate and length of stay, and death compared with people of the same age (38, 41). Consequently, frailty is associated with considerably increased healthcare costs (42). For example, estimates suggest that, during COVID-19, frail older adults accounted for approximately 51% of hospitalized patients with confirmed cases (43), and a systematic review reported that frail individuals had 84% higher odds of future falls compared with non-frail older individuals (44). Despite being associated with increased risk of adverse outcomes and ill-health, frailty is both reversible and dynamic (38) and, thus, prevention and delay of frailty have substantial economic and societal benefits.

1.2.1 Definitions of frailty

How frailty should be best defined has been debated for (39, 45) decades and the complexity of the syndrome makes it difficult to settle on one universal, gold standard definition. There are mainly two schools of frailty: the physical frailty phenotype (40) and the frailty index (46). The physical frailty phenotype definition is grounded in a theoretical construct of predefined clinical features thought to be rooted in an underlying biological basis. The frailty index considers frailty as a non-specific, age-associated accumulation of the total impact of physical, social and psychological exposures acquired over the course of a life.

Physical frailty

Linda Fried and colleagues operationalized the frailty syndrome and proposed a clinical definition of physical frailty in 2001 (40). To date, this is the most commonly used definition (47), also known as 'Fried's (physical) frailty' or 'Fried's phenotype'.

The physical frailty phenotype is based on five distinct characteristics that represent age-associated decline across several physiological systems. These include reduced grip strength and walking speed, self-reported feelings of exhaustion, low physical activity and unintentional weight loss (40). The characteristics are interconnected and can theoretically be unified into a 'cycle of frailty' associated with declining resilience **(Figure 4)**. Fried and colleagues emphasized that frailty probably also involves a decline in reserves or physiological integrity in systems not included in the cycle. The figure illustrates the complexity and dynamic nature of the syndrome, and how a deterioration at any stage may cause a cascade of negative consequences and promote the development of frailty. Notably, the cyclical nature of frailty also enables reversal of the syndrome in the event of an intervention or positive change (38).

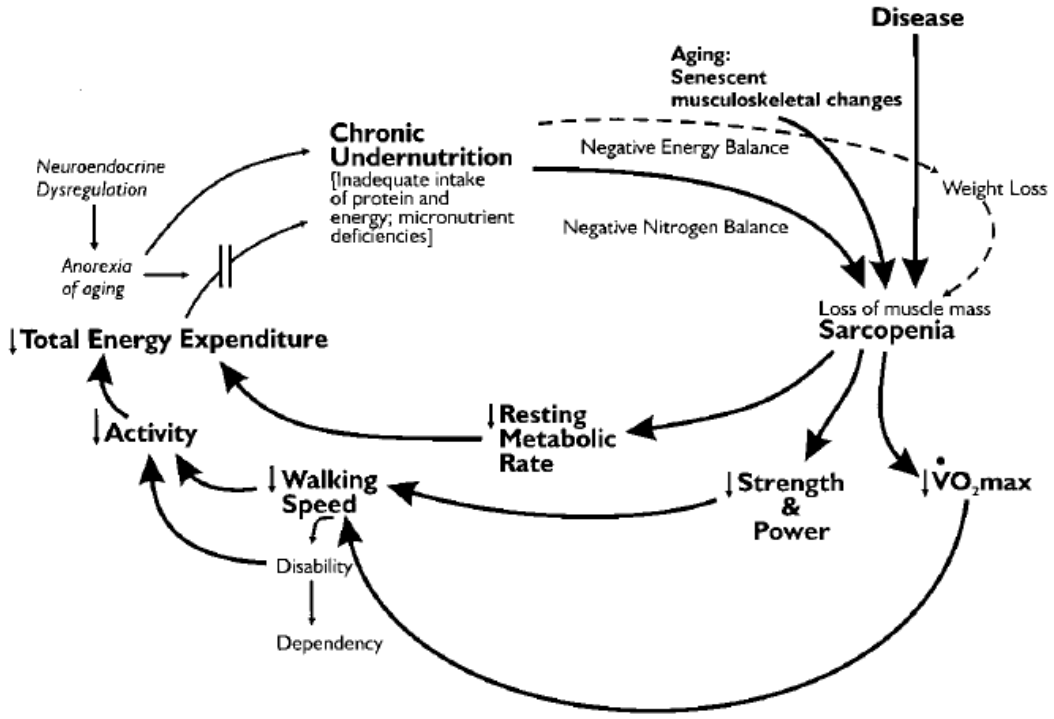

Figure 4 The cycle of frailty. Reproduced with permission from Fried et al. (40), originally from (48).

Using Fried's definition, older adults are classified as 'robust' (not frail) if none of the five characteristics is present, 'pre-frail' in the presence of one or two, and 'frail' in the presence of three or more (40). These three stages are dynamic and reversible (38, 49). Pre-frailty is an intermediate state with increased risk of progression to frailty and adverse health outcomes (50). Physical frailty is not synonymous with either comorbidity or disability, but comorbidity is a risk factor and disability is an outcome of it (40).

Frailty index

The broader definition of frailty is called the frailty index, or the 'accumulation of deficits' method, and was proposed by Mitnitski, Mogilner and Rockwood in 2001 (46). It is based on the principle of counting deficits in health on the grounds that, the more deficits a person has, the frailer that person is (46, 51). As opposed to physical frailty, which should be defined identically regardless of setting and population, there is no requirement that frailty indices contain the same, or the same number of, health deficits, as long as they follow the same conceptual design (52). The health deficits included can be any sign, symptom, disability or disease associated with health and age, as long as they cover a range of systems that, combined, reflects a person's overall health (46). To assess the multifactorial nature of frailty

in a robust way, the frailty index must include a minimum of 30 health deficits (51). Thus, the frailty index is based on the grounds that knowing exactly what is wrong is less crucial than knowing *how many things* are wrong with a person in terms of system behaviour (53).

Typically, the index is expressed as a ratio of the number of deficits present to the total number of deficits considered, presented as a score between 0 and 1 with higher scores indicating a higher degree of frailty (46). The frailty index is preferably used as a continuous variable, but may be dichotomized into frailty/not frailty, typically using typically using a cut-off at frailty index score ≥0.25, which is the most commonly used cut-off in community-dwelling older adults (54).

The use of different and study-specific, modified frailty definitions may contribute to the great variations in observed prevalence (47, 55). According to a systematic review of 21 studies worldwide, overall frailty and pre-frailty prevalence were 11% (range 4–59%) and 42% (range 19–52%) in community-dwelling older adults, respectively (56). In 10 European countries, the overall observed prevalence was 17% for frailty and 42% for pre-frailty in community-dwelling older adults (57). In Norway, previous estimates from the Tromsø Study reported 4% frailty and 38% pre-frailty prevalence in adults aged ≥70 years (58). It is suggested that the risk of frailty varies with socioeconomic factors and geography (47, 59), but – regardless of definition or setting – frailty is more common in women and with advancing age (56, 60).

1.3 Diet and frailty

Diet is one of the main determinants of health (61). The Norwegian Dietary Guidelines (NDG) from 2016 (62) nd the Nordic Nutrition Recommendations (NNR) 2023 (63). define a healthy diet as one rich in whole grains, fruit and vegetables, healthy fats, fish and lean dairy, and low in red and processed meat, sweets and snacks, and alcohol. Eating such a diet should provide an adequate intake of a number of nutrients, including, but not limited to, protein and energy, dietary fibre, unsaturated fatty acids and essential vitamins and minerals – all crucial for good health. Alongside physical activity, diet is one of the few modifiable factors that influence the whole body and multiple systems simultaneously. Studies suggest that a healthy lifestyle and a healthy diet are important to reduce the risk of frailty (64). Conversely, unhealthy diets accelerate ageing and affect key components of the frailty syndrome (65). In recent years, the focus on diet and frailty has increased considerably in epidemiological and clinical research. The following sections give an overview of existing research on diet and

frailty, with emphasis on the dietary factors assessed in this thesis: protein, fish and dietary trajectories.

1.3.1 Nutrients and frailty

Macronutrients

Protein, carbohydrate and fat are the main energy-yielding nutrients (61). Most studies agree that a sufficient, but not excessive, intake of energy is inversely associated with frailty risk in older adults (66-68). Protein and frailty are discussed in detail below.

Carbohydrates are the body's main source of energy, found in cereals, bread, vegetables, fruit, dairy, snacks and confectionary (61). Subgroups of carbohydrates include added sugars and dietary fibres. Added sugars, found in sweets, contribute with little other than energy and are associated with an increased risk of metabolic diseases and dental caries, whereas dietary fibre, found in whole grains and vegetables, contributes to good bowel movements and increased nutrient uptake and is associated with a lower risk of several diseases (61, 63). Three longitudinal studies reported no association between carbohydrate and frailty (69-71), or for added sugars (69) or dietary fibre (70).

Dietary fat, and in particular unsaturated fatty acids, is important for organ protection, energy storage, vitamin transportation and membrane structure; however, studies on total fat and frailty are inconclusive (70-72). Essential fatty acids include the long-chain omega-3 fatty acids (LCn-3FAs), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), found in fatty fish and vegetable oils (63). These fatty acids have anti-inflammatory properties and are associated with reduced cardiovascular disease risk (61). Moreover, studies have suggested that they have beneficial effects on muscle health and mobility in older adults (68, 73-76); however, results from studies on dietary supplementation and frailty are inconclusive (77, 78).

Micronutrients

Micronutrients are ubiquitous in most common foods and include essential vitamins and minerals vital for metabolism and cell function (61). Micronutrient deficiencies lead to malnutrition with detrimental effects on mental and physical health and capacity. Studies agree that micronutrient deficiencies are associated with higher frailty risk (64, 66, 79, 80). In line with this, Bartali et al. observed that a low intake of three nutrients or more increased the risk of frailty (81), and Michelon et al. observed that micronutrient deficiency was more common among frail than non-frail women (82).

Vitamin D, found in fatty fish and fortified dairy products, is crucial for good bone and mental health (63), and deficiency is consistently linked with a higher risk of frailty (82-84). A systematic review concluded that vitamin D supplementation consistently improved strength and balance in adults aged ≥ 60 years (85), although the results are inconclusive on their effect on frailty risk (77, 78). Other micronutrients that have been specifically linked with lower frailty risk include vitamin C (81), vitamin E (86), folate (81, 82), magnesium (87) and carotenoids (79, 82).

Protein and frailty

Protein is the cornerstone construction factor in all living tissues and involved in all bodily processes (61). Dietary protein is used to build and maintain cells and tissues, including muscles and skeleton, and as an energy source. With age, dietary protein intake is crucial to counteract the age-dependent loss of muscle mass and strength. Protein is found in animal foods such as meat, fish, dairy and eggs, and plant sources such as cereals, legumes, nuts and seeds (63). Animal proteins are of higher quality than plant proteins, meaning that they have a more favourable composition and are more efficiently utilized by the human body (61).

Current NDG from 2016 were based on the previous NNR, from 2012 (88). These recommended a daily protein intake of 0.8–1.5 g/kg bodyweight for adults and 1.1–1.3 g/kg bodyweight for older adults, corresponding to 10–20 of the total energy intake (E%) and 15–20 E%, respectively (89). The NNR2023 proposed similar intake of protein E% for adults and older adults, however, the recommended daily protein intake in g/kg bodyweight for older adults differed slightly, at 1.2–1.5 g/kg bodyweight/day (63). The NNR2023 will provide the basis for the new and revised NDG which will be published in 2024, and therefore we assume that the new protein recommendations for Norwegian older adults will similar as in NNR2023.

Protein intake in g/kg bodyweight expresses protein intake in relation to body size and is influenced by changes in bodyweight and/or body composition. Protein intake in E% reflects the proportion of energy from protein in a person's diet, relative to their total energy intake. The E% intake from the different macronutrients informs us of the balance between intakes of macronutrients in the diet, which in turn can reflect the overall quality of the diet, in relation to given recommendations.

Three national dietary surveys, Norkost 1–3, have assessed the diet of the general Norwegian adult population in 1993-4 (90), 1997 (91) and 2010 (92), respectively. These showed that the average adult protein intake in Norway have consistently been in line with dietary recommendations since the 1990's (i.e. in Norkost 1) at around 16–18 E% (90-92). Similarly, in 2021, average protein intake was 16 E% for Norwegian adults (93). Although the differences were minor, the Norkost surveys showed that women and those aged ≥ 60 years have had consistently slightly higher protein intake than men and younger individuals, respectively (90-92). Despite a doubling in meat intake in Norway over the last century, the overall protein intake from animal sources have declined, mainly due to a drastic reduction in dairy and fish intake (94). In Norkost 3, the main protein sources were meat and bread (92).

Protein has been suggested as a key dietary factor in frailty prevention. Insufficient protein intake over time is associated with a greater degree of loss of muscle mass and strength, contributing to weight loss, and ultimately, increased risk of functional decline and frailty (61). Systematic reviews agree that most, but not all, studies show that a higher protein intake is associated with a lower frailty risk in older adults (64, 66, 95-97). Moreover, findings are inconsistent with regard to different protein units assessed (g, g/kg bodyweight, E%). Longitudinal studies have reported inverse associations between protein in g/kg bodyweight (98-101), protein E% (98), and total protein (g/d) (69), and frailty, whereas others found no associations with protein in g/kg bodyweight (67), protein E% (70) and total protein (72, 102). One longitudinal study showed a positive association between total protein intake and frailty in older adults, mainly driven by animal protein (71). In Norway, a longitudinal study showed no association between protein E%, and skeletal muscle mass or hand-grip strength in community-dwelling older adults (103).

Findings from cross-sectional studies are also inconclusive: one study reported an inverse association between quartiles of protein E% and frailty in older adults (104), whereas two studies showed no association between protein in g/kg bodyweight (105, 106) and frailty. Similarly, one cross-sectional study found no association between protein in g/kg bodyweight and physical function in older Norwegian adults (107).

Overall, as there are few longitudinal studies with long follow-up periods on the protein–frailty association, more longitudinal studies are needed to elucidate further the potential role of life-long protein intake on the risk of frailty.

1.3.2 Foods and frailty

Studies have shown that, in addition to nutrients, intake of different foods – and food groups – may be associated with frailty. Three systematic reviews conclude that a higher fruit and vegetable intake appears to be associated with lower risk of frailty (108-110). Findings from prospective studies on intake of dairy products and physical frailty in older adults are inconsistent: two studies reported lower frailty risk from higher intake of low fat dairy (111) and yoghurt (112), while others reported no association between intake of milk (72), low-fat dairy (112), or dairy products (113) and frailty whatsoever. Two sub-studies of the Nurses' Health Study following > 70 000 women aged ≥ 60 years for 22 years reported increased frailty risk from a higher intake of sugar-sweetened and artificially sweetened beverages (114), and unprocessed and processed red meat (115). Conversely, a moderate intake of orange juice was associated with a lower risk of frailty (114).

Fish and frailty

Fish is a rich source of several nutrients important for good health at all ages and a common food group included in definitions of healthy diets (62, 63). Specifically, fish is an important dietary source for the essential LCn-3FAs, high-quality protein, vitamin D, vitamin B_{12}, iodine and selenium, provided one eats both fatty (e.g. salmon, trout, herring, mackerel) and lean (e.g. cod, pollock, tuna) fish. Fatty fish contains more of the LCn-3FAs whereas lean fish is less energy dense but higher in iodine (116). Vitamin B_{12} is important for DNA production and normal nervous function, iodine is a mineral needed for normal thyroid function and metabolism and selenium is important for protection from oxidative damage and infection (61). In particular, for LCn-3FAs, vitamin D and iodine, there are very few other natural sources in the diet (61). Notably, fish may also contain several contaminants such as methylmercury and organic pollutants, and it has been debated whether a frequent fish intake introduces harmful intake levels of these and the potential consequences. However, a recently published benefit and risk assessment of fish intake in the Norwegian diet concluded that the positive health effects from increasing fish intake to the recommended two to three dinners per week outweigh the risks for all age groups (117).

Current NDG and the NNR2023 recommend eating fish for dinner two to three times a week and to use fish as a spread on bread. This amounts to a weekly intake of 300–450 g of prepared fish for adults, of which at least 200 g should be fatty fish (63, 116). Fishing has always been important in Norway. With its long coastline and longstanding fishing tradition, fish has traditionally been an important part of the Norwegian diet (118). However, this trend

is turning because fish intake in Norway has gradually declined over the last century (93). In Norkost 3 (2010), average adult weekly fish consumption was 238 g (110 g of fatty fish) among women and 350 g (134 g of fatty fish) among men (92). Findings from Norkost 1–3 (1993–2010) have shown that men consistently ate more fish than women, fish intake increases with age and higher education, and fish intake is higher in Northern Norway compared with the rest of the country (90-92).

Systematic reviews have concluded that diets including fish are associated with lower frailty risk (64, 66, 119). Moreover, results from intervention and longitudinal studies suggest that the intake of lean (120) and fatty fish (121) are associated with improved muscle mass and function (120), and lower accumulation of age-related health deficits (121) in older age, respectively. Cross-sectional studies have suggested an independent inverse association between higher intake of total and fatty fish and frailty (122-124). In addition, cross-sectional studies have showed positive associations between fatty fish intake and improved grip strength (125), and fish intake and higher walking speed in older adults (107).

However, there are few longitudinal studies on fish and frailty as such, and the results are inconsistent with regard to the effects of different categories of fish (fatty, lean and total fish) on health in older adults. Moreover, no study has specifically investigated the association between different patterns of habitual fish intake and later health outcomes.

1.3.3 Dietary patterns and frailty

In dietary research, dietary patterns have gained considerable attention over the past decades. The main argument for this is that intakes of foods and nutrients are related, because people do not consume single foods or nutrients, but combinations of foods (126). Similarly, the focus in diet–frailty research has shifted from focusing on single nutrients to investigating the role of the overall diet and dietary patterns in frailty development (119, 127).

Data from the Norkost dietary surveys showed that between 1993–2010, the average E% from dietary protein, carbohydrates, added sugars, fat and alcohol was in line with the NDG and the NNR2023 (62, 63, 90-92). However, the diet contained consistently too much saturated fat and too little dietary fibre (90-92). In Norkost 1 (1993–94) and 2 (1997), about 10–12 % met the recommendation of eating five or more servings of fruit and vegetables per day (90, 91). In Norkost 3 (2010), the proportion was slightly higher, because 14% ate ≥250 g vegetables daily and 38% ate ≥250 g fruit daily (92). Those with higher education and higher

socioeconomic status consistently had a somewhat healthier diet than those with lower education and a lower socioeconomic status (90-92).

A systematic review from 2019 on dietary patterns and frailty concluded that a diet high in fruit, vegetables and whole grains may be associated with a reduced risk of frailty – mostly defined using Fried's definition (119). In line with this, longitudinal (128, 129) and cross-sectional (130-132) studies have reported an inverse association between higher diet quality and frailty, defined using the frailty index. Similarly, other longitudinal studies have shown that higher consumption of healthy plant foods, including whole grains, fruit, vegetables, legumes and nuts, was associated with a lower risk of frailty (133, 134) and accelerated ageing (135) in community-dwelling older adults, whereas the opposite was seen for diets characterised by unhealthy plant foods.

Adherence to the Mediterranean diet appears to have a beneficial effect on frailty prevention and promotion of healthy ageing, although there is some heterogeneity in the results from studies investigating this (132, 136-139). Furthermore, adherence to a healthy Nordic diet was associated with better overall physical performance in older Finnish women (140), and prolonged lifespan with good mental and physical health in Swedish older adults (141).

Different diets have been investigated in these studies, however, in essence they are all characterized by high intakes of vegetables, fruit, whole grains, legumes, healthy fats and oils, moderate intakes of dairy and fish, and low intakes of red and processed meat, unhealthy fats, sweets and snacks – very much in line with the NDG and the NNR2023 (62, 63). Thus, there seems to be an overall preventive effect on frailty from adhering to dietary guidelines or comply with healthy dietary patterns.

Dietary trajectories and frailty

Although many studies have investigated the associations between diet and frailty, in most of these, dietary intakes are assessed at a single time point. However, as it is increasingly recognized that people's food preferences and dietary choices can change over time, life situation and age, interest in the effect of long-term diet on health has gained increased attention over the past decade (142, 143). In addition, time periods when individuals experience significant dietary changes are also distinguishable when diets are measured over an extended time frame, which may provide information about when and in whom to intervene with nutritional interventions (142).

Methods to evaluate diet over time include dietary tracking and dietary trajectories. Although these terms may often be used interchangeably, tracking can be defined as the stability of a certain risk factor over time (144), whereas trajectories reflect distinct – and possibly complex – patterns over time (142). Patterns in dietary tracking are typically identified manually by the researcher via cross-tabulation, whereas dietary trajectories are often identified using statistical methods such as the group-based trajectory modelling (GBTM). This identifies latent patterns among the participants in the dataset and allows for individual variation over time (142, 145).

Most studies on dietary trajectories are performed in children and adolescents, typically focusing on the transition periods from infancy to childhood, adolescence and adulthood (142). There are fewer studies in adults and older adults, most probably because this is considered a more 'set' population, with individuals who are less open to interventions and changing their diet. However, recent studies on dietary trajectories during adulthood suggest that changes in patterns of dietary intake even during mid-adulthood, may have consequences for many chronic conditions later in life (142). There are no previous studies on dietary tracking or on dietary trajectories and frailty. However, there are studies on dietary trajectories and frailty-related health outcomes in adults and older adults. For example, one study showed that improving diet quality in mid-life was associated with better physical function in older age (146). Moreover, studies have reported that patterns of consistently high or improved dietary quality over time were associated with later improved cardio metabolic outcomes (147-150), cognitive health (151, 152), psychosocial well-being (151) and lower mortality (153, 154).

1.4 Methods in nutritional epidemiology

Nutritional epidemiology is the study of the relationship between dietary factors and health and disease (155). Although methodological advancements in the nutritional epidemiological field have grown over the past decades, critics remain sceptical about its methods, interpretation and reliability of results. Much of the criticism concerns the inability to accurately measure diet and its reliance on observational studies (156). Observational studies cannot establish causality, but may provide estimates of association between cause and effect (157). For causality, one needs randomized controlled trials (RCTs), generally considered to be the gold standard in research study design for determining causal relationships (158). However, it is often impossible or not feasible to carry out RCTs that will answer all

nutritional epidemiological questions. RCTs are often costly and invasive, with shorter follow-up, and may have ethical and methodological challenges. Conversely, observational studies with large sample sizes and long follow-up periods allow for a broader view on the relationship between diet and multiple health outcomes and are preferable when studying long-term dietary intake and diet–disease associations in humans (155, 156).

1.4.1 Methods for assessing dietary intake

Dietary assessment methods are an ever-evolving field within nutritional research, constantly striving towards increasingly accurate and non-invasive methods (159). Traditional methods of dietary assessment include prospective and retrospective methods such as self-reported food records and diaries, food frequency questionnaires (FFQs) and 24-hour recalls. The choice of method should reflect the population, setting, time frame and purpose of research (160).

Food frequency questionnaires

The FFQ is the most frequently used method to assess dietary intake in larger epidemiological studies, including the studies in this thesis. It is a retrospective method that assesses habitual intake over a specific period of time, e.g. a month or a year (160, 161). The FFQs are typically self-reported by the individuals and include questions on how frequent, and often also how much, one eats different foods. FFQs can be qualitative, semi-quantitative or quantitative. Qualitative FFQs asks only about frequencies of intake, semi-quantitative FFQs include standard portion sizes and quantitative FFQs ask about the exact amounts eaten (159). The last is associated with a higher participant burden, but, overall, self-reported FFQs are a non-invasive and cost-effective dietary assessment method. The quality and reliability of the collected data are only as good as the FFQ used and it is therefore vital that the questions are suitable for the specific population, setting and research questions (160, 161).

Handling of dietary data

The level of processing of collected dietary data before analysis depends on the nature of the data and the purpose of the study. Generally, dietary data may be used and analysed at three levels of intake: 1) frequency of food and drink intake; 2) quantity of food and drink intake; and 3) estimated intake of micro- and macronutrients (159, 161).

When assessing frequencies of intake, the collected data can most often be analysed as they are, without any additional processing (161). If the focus is on quantities of intake, the

reported frequency and portions of the specific foods consumed are combined to estimate a daily intake, typically presented in g per day. For these calculations, tables with standard weights and average portions for common foods are used, alongside food-labelling information for foods for which standard weights are not available. Third, for analyses on nutrient intake, a designated food and nutrient calculation system connected to a food composition table is required (161).

Defining dietary patterns

In dietary research, dietary patterns are derived via two methods: either *a priori* – based on existing knowledge of diet–disease relationships – or *a posteriori*, using data-driven methods to identify dietary patterns and behaviour among individuals in a specific population (159).

Using *a priori* methods, individuals are typically scored based on their adherence to recommended dietary guidelines or predefined dietary patterns, ranging from – most frequently – least healthy to most healthy (159). Thus, the scores aim to reflect risk gradients for major diet-related diseases (162). Examples of well-known diet scores include the Mediterranean Diet Score (MDS) and the Alternative Healthy Eating Index (AHEI), which measure adherence to the Mediterranean diet (163) and the Dietary Guidelines for Americans with emphasis on chronic disease risk reduction (164), respectively. Two critical reviews on common predefined diet quality scores and their construction criteria concluded that the scores differed greatly in several aspects, including the items included, the exact method of scoring, the cut-off values used and the weighting of the relative contributions of the individual components to the total score, suggesting that many arbitrary choices were made (126, 162). Thus, as for FFQs, the quality of a diet score depends on the evidence base on which it is based and how thorough the construction process of the score has been. In addition, the choice of diet score must be suitable for the population in which it is to be used.

The *a posteriori* method involves statistically derived patterns from collected dietary data based on correlations in intakes of the various dietary components (159). Consequently, the patterns derived are study-specific and do not take health or dietary recommendations into account.

1.5 Knowledge gap

Most previous studies on diet and frailty have had cross-sectional designs or short follow-up periods (66, 108). Consequently, frailty may already be present in the participants, which could influence food choices and preferences (64). Researchers are consistently calling for more high-quality studies with longer follow-up periods on diet and frailty (119, 165), and the literature is particularly scarce on diet through time (i.e. tracking and trajectories) and frailty. Moreover, existing dietary research is dominated by studies on physical frailty, as defined by Fried et al. (40), with fewer studies focusing on the pre-frailty phase of the syndrome (79), or frailty defined using the frailty index of Rockwood et al. (97, 166).

2 Aims

The overall aim of this thesis was to advance the field of diet and frailty by investigating the longitudinal association between diet in adulthood and into old age, and frailty status in Norwegian older adults. It aimed to analyse the association by investigating the influence of relevant dietary components measured at single time points, and tracked as patterns of intake over time.

The specific aims of the papers were as follows:

- To analyse the association between previous and current daily intake of protein, as well as tracking patterns of protein intake over 21 years, and pre-frailty/frailty (Paper I).
- To investigate the association between lean, fatty and total fish intake and pre-frailty 8 years later, and to investigate the association between consistent patterns of total fish intake over 21 years and pre-frailty (Paper II).
- To investigate the association between trajectories of diet over 21 years and frailty (Paper III)

3 Methods

3.1 Study design and setting

3.1.1 The Tromsø Study

Tromsø is the largest municipality in Northern Norway. Its approximately 77 700 inhabitants (2022 data) (167) are dominated by white, mainly Norwegian origin (85%), alongside a Sami minority, and may be considered as representative of a northern European urban population (168).

The present thesis used data from the Tromsø Study, Norway's largest population-based study, affiliated with UiT, The Arctic University of Norway. The first study, 'The Tromsø Heart Study', was initiated in 1974 as a response to the cardiovascular disease epidemic in Northern Norway (168, 169). Since then, seven cross-sectional surveys (Tromsø1 to Tromsø7) have been conducted every 7–8 years and the focus has expanded to a broad range of chronic diseases (169). This thesis used data from Tromsø4 (1994–95), Tromsø5 (2001), Tromsø6 (2007–08) and Tromsø7 (2015–16).

Study design in the Tromsø Study

Based on the official population registry available at the time of the seven surveys, total birth cohorts and random samples of the Tromsø population were invited to participate. From Tromsø5 onwards, previous participants were invited as a priority (168). Participation rates have ranged between 65% and 79% and, altogether, 45 473 men and women have participated in one or more of the surveys (168, 170).

All surveys have had similar overall design. In each survey, the invited Tromsø residents received an information leaflet and a personal invitation to the study (visit 1) by mail. From Tromsø4 onwards, subsamples of the participants were also invited to a second visit (visit 2) for additional and more comprehensive examinations. Due to lack of funding and capacity, not all participants could be invited to visit 2, but in each survey, subgroups of participants eligible for visit 2 were identified before study enrolment (168). However, Tromsø4 participants who attended visit 2 would consistently be invited to both visit 1 and 2 in the later Tromsø surveys, to facilitate repeated study participation. Eligible participants had to attend visit 1 to be invited to visit 2 (168). The following sections focus on Tromsø4 to Tromsø7, the surveys included in this thesis.

3.1.2 Data collection

A brief overview of the non-dietary data used in Paper I–III from Tromsø4 to Tromsø7 is presented in **Table 1**. An updated, comprehensive list of all variables collected is available online at https://helsedata.no/en/variables/?datakilde=K_TR&page=search.

In all surveys, a short questionnaire was provided alongside the invitation. This questionnaire was to be completed at home and brought to visit 1. On attendance, participants were given a second, more comprehensive questionnaire which was to be completed either on-site or at home and returned by mail. With time, the questionnaires have evolved to cover a broad range of topics, including symptoms, diseases, use of medication and healthcare services, family history of disease, dietary habits and lifestyle, beliefs and attitudes, socioeconomic status and quality of life. All questionnaires are available at the Tromsø Study's webpages (169). To supplement the information obtained from the questionnaires, a short interview was included in the surveys.

At visit 1, the participants underwent physical and clinical examinations. The number of measurements has increased over time, but, in all surveys, height (cm) and weight (kg) were measured with light clothing and no shoes. Visit 2 included additional measurements of physical function, balance and standard blood and urine tests and, from Tromsø5 onwards, cognitive function (168).

Table 1 Variables used in Papers I–III from Tromsø4–Tromsø7

	Tromsø4 (1994–95)	Tromsø5 (2001)	Tromsø6 (2007–08)	Tromsø7 (2015–16)
Questionnaire data				
Age, sex	x	x	x	x
Marital status, living situation	x	x	x	x
Smoking habits	x	x	x	x
Physical activity	x	x	x	x
Self-rated health	x	x	x	x
Education	x	x	x	x
Support of friends	x	x	x	x
Alcohol consumption	x	x	x	x
Diseases (past or present)	x	x	x	x
Unintentional weight loss			x	x
Feeling exhausted			x	x
Mobility and functionality			x	x
Dental health				x
Medication use				x
Number of falls				x
Depression and attitudes				x
Sleep				x
Measured data				
Height, weight	x	x	x	x
Waist, hip circumference				x
Haemoglobin levels				x
Grip strength test			x	x
Walking speed test				x
Physical function test				x
Cognitive testing			x	x
Spirometry				x

FFQ, food frequency questionnaire.

3.1.3 Surveys

Tromsø4 (1994–95)

In the fourth Tromsø survey, all 37 558 Tromsø residents born before 1970 (i.e. ≥ 25 years) were invited, of whom 27 158 (77%) participated. On attendance, slightly different questionnaires were given to participants aged < 70 and ≥ 70 years. Among participants, everyone aged between 55 and 74 years, along with 5–10% of those in the 25–54 and 75–85 age groups, were invited to visit 2. A total of 7965 attended visit 2, 76% of those invited (169).

Tromsø5 (2001)

In the fifth survey, 10 535 men and women aged 30–89 years were invited and 8130 (79%) participated (168). Those invited were mostly men and women who had previously participated in visit 2 in Tromsø4, alongside subgroups of people in the age groups 30, 40, 45, 60 and 70 years (169). As in Tromsø4, participants younger and older than 70 years received somewhat different questionnaires. In total, 5039 previous Tromsø4 participants took part in visit 2 (85% of those invited).

Tromsø6 (2007–08)

In the sixth Tromsø survey, 19 762 were invited and 12 984 (66%) men and women aged 30–87 participated (171). Invitations were sent to previous Tromsø4 participants, a 10% random sample aged 30–39, all individuals aged 40–42 or 60–87 years and a 40% random sample aged 43–59 years. To visit 2, all participants aged 50–62 and 75–84 years, a 20% random sample of participants aged 63–74 years and, if not already included in the two groups, previous participants in Tromsø4 were invited, of whom 7307 (63%) participated (171).

Tromsø7 (2015–16)

In the seventh survey, all 32 591 Tromsø residents aged ≥ 40 years were invited and 21 083 (65%) participated. Eligible participants for visit 2 included a 20% random sample of individuals aged 40–59 years and a 50% random sample aged 60–84 years, plus previous participants. In total, 8346 (90%) participated (170).

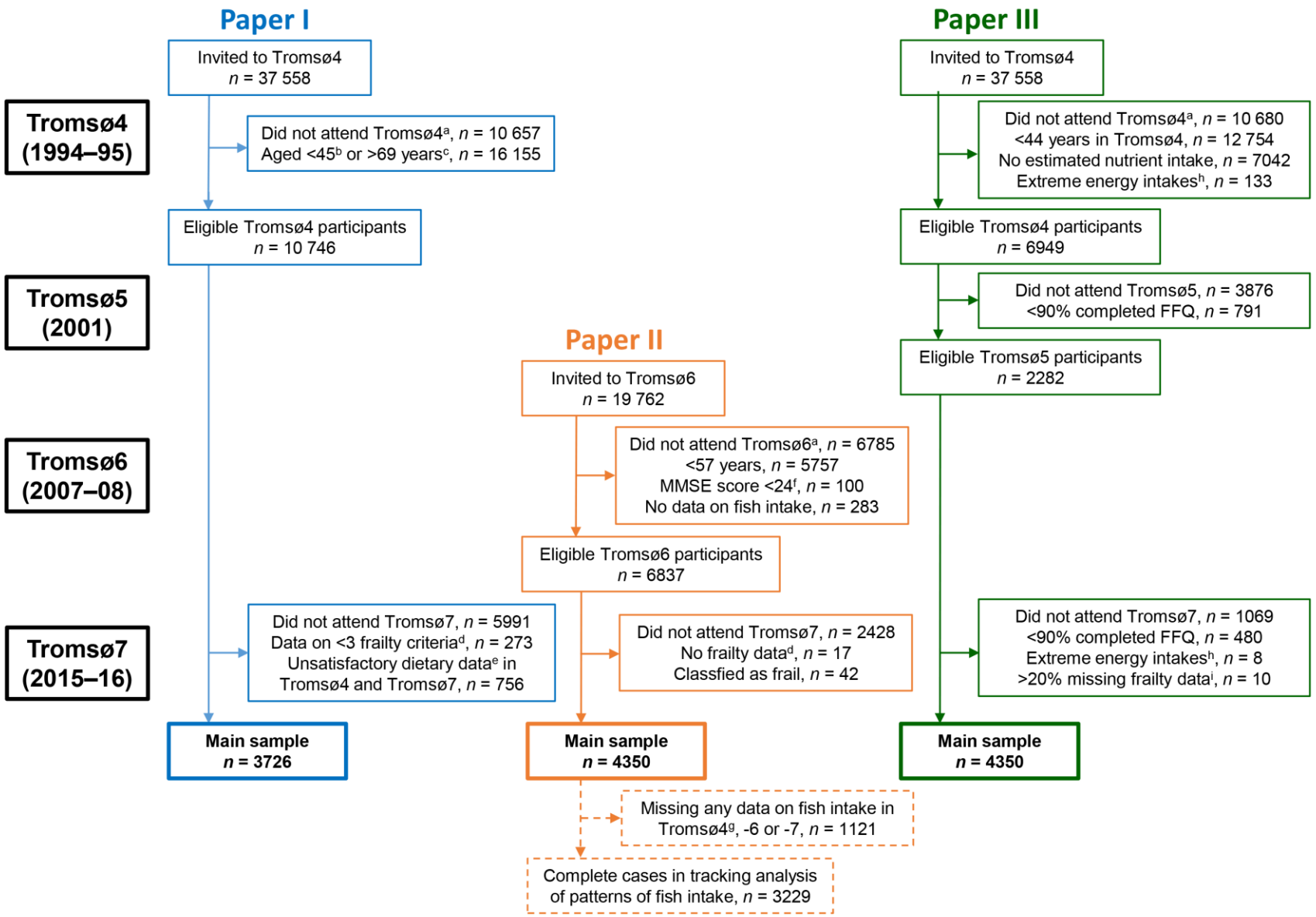
Paper I
Paper II
Paper III
Tromsø4 (1994–95)
Tromsø5 (2001)
Tromsø6 (2007–08)
Tromsø7 (2015–16)
Invited to Tromsø4 n = 37 558
Did not attend Tromsø4a, n = 10 657
Aged <45b or >69 yearsc, n = 16 155
Eligible Tromsø4 participants n = 10 746
Invited to Tromsø6 n = 19 762
Did not attend Tromsø6a, n = 6785
<57 years, n = 5757
MMSE score <24f, n = 100
No data on fish intake, n = 283
Eligible Tromsø6 participants n = 6837
Did not attend Tromsø7, n = 5991
Data on <3 frailty criteriad, n = 273
Unsatisfactory dietary datae in Tromsø4 and Tromsø7, n = 756
Did not attend Tromsø7, n = 2428
No frailty datad, n = 17
Classfied as frail, n = 42
Main sample n = 3726
Main sample n = 4350
Missing any data on fish intake in Tromsø4g, -6 or -7, n = 1121
Complete cases in tracking analysis of patterns of fish intake, n = 3229
Invited to Tromsø4 n = 37 558
Did not attend Tromsø4a, n = 10 680
<44 years in Tromsø4, n = 12 754
No estimated nutrient intake, n = 7042
Extreme energy intakesh, n = 133
Eligible Tromsø4 participants n = 6949
Did not attend Tromsø5, n = 3876
<90% completed FFQ, n = 791
Eligible Tromsø5 participants n = 2282
Did not attend Tromsø7, n = 1069
<90% completed FFQ, n = 480
Extreme energy intakesh, n = 8
>20% missing frailty datai, n = 10
Main sample n = 4350

Figure 5. Flow chart of study participants from Tromsø4–Tromsø7 included in the analyses in Papers I–III.
FFQ, food frequency questionnaire; MMSE: Mini-Mental Examination.
[a]Includes participants who at any point withdrew their consent to participate. The Tromsø Study dataset is continuously updated and participants who withdraw their consent after participation are deleted from the dataset retrospectively. Therefore, the number of participants included in datasets used in Papers I and III differs.
[b]Age cut-off incorrectly set to ≥45 instead of ≥44 years in Paper I.
[c]Participants aged ≥ 70 years in Paper I were excluded because they did not have data on estimated dietary intake.
[d]Fried's frailty.
[e]No data on estimated nutrient intakes in Tromsø4 or < 90% completed FFQ in Tromsø7.
[f]Cut-off for normal cognitive function in community-dwelling older adults.
[g]Extracted data on fish intake in Tromsø4 among participants within main sample.
[h]Outside < 1st and > 99th percentiles of estimated energy intake.
[i]Frailty index.

3.1.4 Study populations

The present work includes subgroups of adult men and women from the last four surveys of the Tromsø Study, selected according to the study-specific aims of the papers included in the thesis. A flow chart of participants included in Paper I–III is presented in **Figure 5**.

Paper I

This study included participants from Tromsø4 aged 45–69 years who also participated in Tromsø7 and had data on a minimum of three out of five frailty criteria in Tromsø7. Participants without valid estimated protein intake in either Tromsø4 or Tromsø7 were excluded, as were participants with energy intakes outside the < 1st and > 99th percentiles at either time point. In total, 3 726 participants constituted the main analytical sample. We discovered in hindsight that, in Paper I, the age cut-off for inclusion in Tromsø4 was incorrectly set to ≥ 45 years (≥ 66 years at follow-up), when it should have been ≥ 44 years (and ≥ 65 years). However, this had no implications on the results, as the observed associations were similar regardless of which of these age-cut off used (data not shown). This error was corrected in the following papers.

Paper II

In the second study, the baseline was set to Tromsø6 and participants were included if they were aged ≥ 57 years, had data on frequency of either lean or fatty fish intake and had a Mini-Mental State Examination (MMSE) score ≥ 24. In Tromsø7, we excluded those without any frailty data and those classified as frail, leaving 4350 participants for the main analysis. Among these, a subsample of 3229 participants with complete data on fish intake in Tromsø4**,** Tromsø6 and Tromsø7 was identified for tracking analysis of patterns of fish intake over 21 years (dashed box in **Figure 5**).

Paper III

This study included participants aged ≥ 44 years in Tromsø4 who also participated in Tromsø5 and Tromsø7. Participants were excluded if they did not have data on estimated nutrient intakes in Tromsø4 or completed < 90% of the FFQ in Tromsø5 or Tromsø7, if they had estimated energy intakes outside the < 1st and > 99th percentiles in Tromsø4 or Tromsø7, and if they had > 20% missing frailty data in Tromsø7. In total, 715 participants were included in the analysis.

3.1.5 Ethics

The Tromsø Study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants, and data from participants who withdrew their consent were excluded before data delivery from the Tromsø Study. The PhD project was approved by Regional Committees for Medical and Health Research Ethics (REK: 2019/43798).

3.2 Assessment of frailty

3.2.1 Physical frailty

In Papers I and II, frailty in Tromsø7 was defined using a modified version of Fried's phenotype. A comparison of the measurement instruments used to define physical frailty used in Tromsø7 versus those used by Fried et al. in 2001 is presented in **Table 2**, and in more detail in **Supplementary Table S1** in Paper I.

Table 2 Measurements of frailty characteristics in Tromsø7 and by Fried et al. (40).

Characteristics	**Measurement in Tromsø7, 2015**	**Measurement by Fried et al., 2001**
Weight loss	Self-reported, based on the Malnutrition Universal Screening Tool (172).	Self-reported or measured at follow-up.
Exhaustion	Self-reported, based on the Hopkins Symptoms Checklist 10 (173).	Self-reported, based on the Center for Epidemiologic Studies Depression Scale (174).
Physical activity	Self-reported, based on Saltin–Grimby Physical Activity Level Scale (175).	Self-reported, based on the Minnesota Leisure Time Activity short questionnaire (176).
Walking speed	Measured at visit 2 with Short Physical Performance Battery walking test (177).	Fifteen-foot walk test.
Grip strength	Measured at visit 2 using a Jamar dynamometer (178).	Measured using a Jamar dynamometer.
Frailty score	0 = not frail/robust, 1–2 = pre-frail, ≥ 3 = frail	

Using the measurement instruments presented in **Table 2**, physical frailty in Tromsø7 was defined accordingly:

1. Unintentional weight loss was defined as any involuntary weight loss during the last 6 months.
2. Exhaustion was defined as answering 'Pretty much' or 'Very much' to the question 'Have you felt that everything is a struggle during the last week?'.

3. Low physical activity was defined as selecting the lowest level of activity: 'Mainly reading, watching TV/screen or other sedentary activity' as a description of one's average leisure activity level during the previous year.
4. Walking speed defined as seconds (s) spent walking 15 feet, stratified by sex and height (in cm).

Men	*Women*
Height ≤ 173 & ≥ 7 s	Height ≤ 159 & ≥ 7 s
Height > 173 & ≥ 6 s	Height > 159 & ≥ 6 s

5. Weakness was defined as maximal grip strength (kg), stratified by sex and BMI.

Men	*Women*
BMI ≤ 24 & ≤ 29 kg	BMI ≤ 23 & ≤ 17 kg
BMI 24.1–26 & ≤ 30 kg	BMI 23.1–26 & ≤ 17.3 kg
BMI 26.1–28 & ≤ 30 kg	BMI 26.1–29 & ≤ 18 kg
BMI > 28 & ≤ 32 kg	BMI > 29 & ≤ 21 kg

Body mass index (BMI) was calculated as body weight in kilograms divided by the square of height in metres (kg/m^2). All five frailty characteristics were dichotomized. Participants with three or more criteria present were classified as frail, those with one or two were classified as pre-frail, whereas participants with no criteria present were classified as robust (or 'non-frail'). As there were few participants with physical frailty in Tromsø7, to facilitate meaningful analyses, frail participants were combined with the 'pre-frail' group in Paper I and excluded in Paper II. Thus, the outcomes assessed were, not 'frailty' as such, but rather 'pre-frailty/frailty' (Paper I) and 'pre-frailty' (Paper II).

3.2.2 Frailty index

In Paper III, frailty in Tromsø7 was defined using a 41-item frailty index. The frailty index consisted of 41 self-reported and objectively measured health deficits in Tromsø7, covering different aspects of health: diseases and medication use (n = 15), objective physical measures (n = 6), self-reported health and function (n = 8), motivation and attitudes (n = 4), vitality and quality of life (n = 5), and cognition and memory (n = 3). An overview of the deficits included in the frailty index is presented in **Table 3**. Each health deficit was given a score between 0 (not present) and 1 (fully present). The frailty index was then calculated as the proportion of health deficits present in an individual out of the total number of deficits measured, resulting in a score ranging from 0 (least frail) to 1 (extremely frail). We allowed for 20% missing data

in the frailty index (51), translating to missing data on maximum eight out of 41 variables ($41 \times 20\% = 8.2$). Thus, all participants included in the analyses had data on at least 32 health deficits. For example, if a participant had 12 deficits present out of a total of 35 deficits measured, because data on 5 health deficits were missing, the frailty score would be $12/35 = 0.34$. For descriptive purposes, the frailty score was dichotomized to frail versus not frail by cut-off ≥ 0.25 (54).

Table 3 Health deficits included in the frailty index in Tromsø7

No.	Health deficits in main categories
	Diseases and medication use
1	Diabetes
2	Cancer
3	Stroke
4	Cardiovascular disease
5	Pulmonary disease
6	Inflammatory disease
7	Incontinence
8	Indigestion/abdominal pain
9	Severe/chronic pain
10	Thyroid hormone medicines
11	Hearing impairment
12	Other disease
13	Psychological problems
14	Polypharmacy (≥5 medications daily)
15	Low haemoglobin levels (g/dl)
	Objective physical measures
16	SPPB: balance test (s)
	Feet-gathered posture
	Semi-tandem posture
	Tandem posture
17	SPPB: walking speed (s/m)
18	SPPB: chair stand test (s)
19	Grip strength (kg)
20	Waist circumference (cm)
21	BMI outside normal (22–27 kg/m^2)

No.	Health deficits in main categories
	Self-reported health and function
22	Own health in general
23	Own health compared to others of same age
24	Own dental health
25	Falls previous year
26	Unintentional weight loss previous 6 months
27	Mobility (walk about)
28	Self-care (dress and wash)
29	Usual activities
	Motivation and attitudes
30	Depression
31	Anxiety
32	Feeling that everything is a struggle
33	Not feeling happy
	Vitality and life quality
34	Problems sleeping
35	Life satisfaction
36	Feeling hopeless about the future
37	Lacking good friends
38	Not believing in self
	Cognition and memory
39	MMSE score
40	Impaired memory
41	Problems with daily tasks

BMI, body mass index (kg/m^2); MMSE, Mini-Mental State Examination; SPPB, Short Physical Performance Battery.

3.3 Assessment of diet

3.3.1 Dietary assessment in the Tromsø Study

Dietary information in the Tromsø Study was self-reported in the questionnaires. Over time, the scope of dietary data collected in the Tromsø Study has increased from only a few diet-related questions in the questionnaires to a separate, 13-page FFQ in Tromsø7 (**Table 4**). As different questionnaires were given to participants aged < 70 and ≥ 70 years in Tromsø4 and Tromsø5, the dietary data collected were slightly different for these two age groups. Overall, the questions have covered meal patterns, food preferences, frequency and/or amount of intake of different foods and drinks. Some foods have been covered consistently in all surveys, including coffee and tea, potatoes, juice, sugary drinks and fatty fish. Alcohol intake

and dietary supplements were also asked about in all surveys. Other than this, the surveys varied greatly in the number, type and wording of the food-related questions and their accompanying answer alternatives. Tromsø4 and Tromsø7 have the most comprehensive dietary data and are the only surveys with estimated nutrient intake.

Table 4 Dietary assessment in Tromsø4–Tromsø7

Dietary questions[a]	**Tromsø4 (1994–95)**	**Tromsø5 (2001)**	**Tromsø6 (2007–08)**	**Tromsø7 (2015–16)**
Questionnaires, questions	38[b], 25[c]	25[b], 20[c]	39	37
FFQ, questions				261

FFQ, food frequency questionnaire.

[a]Does not include questions on alcohol consumption and dietary supplement use.

[b]Participants aged < 70 years.

[c]Participants aged ≥ 70 years.

Tromsø4

In Tromsø4, dietary data were collected through 38 food-related questions (**Table 4**). The questions covered food and drinks such as bread, milk, yoghurt, snacks and sweets, fruit, vegetables, lean, fatty and processed fish, meat, spreads, eggs and type of fat used in cooking and on bread. Of these, 34 covered energy-yielding foods that provided the basis for estimated energy and nutrient intake. Jacobsen and Nilsen have described the dietary estimation in Tromsø4 in detail previously (179). In short, nutrient calculations were performed only for participants aged < 70 years who had answered a minimum of 31 (90%) of the relevant questions. Sex-specific portion sizes for different foods were estimated based on data from previous dietary surveys conducted in Northern Norway (180, 181). The intakes of food groups were calculated using recipes that reflected the local food items in the specific food groups (179). The nutrient intakes were estimated using the Norwegian food composition table of 1995 (182), supplemented with data from the corresponding Swedish food composition table (183).

Tromsø5

In Tromsø5, dietary data were collected through 25 questions (**Table 4**). Of these, 22 questions concerned frequency of intake whereas 3 asked about preferences, including type of fat used on bread/in cooking. The frequency questions covered fruit and berries, cheese, potatoes, boiled and fresh vegetables, fatty fish, juice, water, different types of milk, soft drinks, tea and coffee.

Tromsø6

In Tromsø6, dietary data were collected through 39 frequency questions, covering fruit, vegetables, potatoes, pasta/rice, meat, lean and fatty fish, milk/yoghurt, juice, tea, coffee, hot chocolate, chocolate and cakes (**Table 4**).

Tromsø7

In Tromsø7, dietary data were collected through 37 frequency questions, and a 261-item FFQ developed at the University of Oslo (UiO) (Table 4). The frequency questions covered common foods such as fruit, vegetables, fish, meat, milk, juice, soft drinks and, similar to Tromsø6, foods containing toxins and heavy metals. The FFQ was, however, designed to cover a person's total diet in the last year, including questions on 261 different foods, dishes, meals and beverages. The nutrient estimation based on the FFQ has been described in detail by Lundblad et al. (184). Briefly, daily nutrient intakes were calculated with the food and nutrient calculation system KostBeregningssystem (KBS), version 7.3 (database version AE14) at the UiO. The KBS AE14 is based on the 2014–15 version of the Norwegian food composition table (https://www.matvaretabellen.no/?language=en), supplemented with data from other databases and calculated recipes (184).

3.3.2 Dietary variables in Papers I–III

The dietary variables included in the different papers depended on the specific study aims and are presented in **Table 5**. The handling of the dietary variables is described in more detail in the specific papers.

Table 5. Dietary variables from the Tromsø Study analysed in Papers I–III.

	Tromsø4 (1994–95)	**Tromsø5 (2001)**	**Tromsø6 (2007–08)**	**Tromsø7 (2015–16)**
Paper I	Estimated daily energy and protein intake			Estimated daily energy and protein intake
Paper II	Frequency of lean and fatty fish intake		Frequency of lean and fatty fish intake	Frequency of lean and fatty fish intake
Paper III	Estimated macronutrient intake Data from 31 frequency and food preference questions	Data from 19 frequency and food preference questions		Estimated micro- and macronutrient intake from 261-item FFQ Data from 3 frequency questions

FFQ, food frequency questionnaire.

Paper I: protein intake

The estimated daily protein intake measured at baseline (Tromsø4) and follow-up (Tromsø7) in Paper I was analysed as relative to bodyweight (g/kg bodyweight) and relative to estimated energy intake (g/megajoule (MJ)).

Paper II: fish intake

In Paper II, the fish intake measured in Tromsø4, Tromsø6 (baseline) and Tromsø7 (follow-up) was based on two questions on frequency of intake of lean and fatty fish. Each question was originally accompanied by five or six answers, i.e. intervals for intake frequencies, ranging from '0–1 times a month' to '1–2 times a day'. The answer alternatives on frequency of intake differed slightly between the surveys (detailed overview of questions in **Supplementary Table S1**, Paper II). Frequency of lean, fatty and total fish intake was assessed in Tromsø6, whereas total fish intake was assessed in Tromsø4, Tromsø6 and Tromsø7, organized into patterns of fish intake over time ('tracking analysis'). The variable total fish intake was constructed as the sum of self-reported intake of lean and fatty fish at each time point.

Paper III: construction of diet scores

All dietary variables included in Paper III were included in three distinct diet scores, one in each survey (Tromsø4, Tromsø5 and Tromsø7). The constructional basis for the diet scores was the recently published NNR for intake of nutrients and food groups (63). Detailed overviews of the rationale, contents and scoring of the diet scores are presented in **Supplementary Tables S1** and **S2** in Paper III. Cut-offs for dietary intake were set according to the NNR2023, supplemented with cut-offs and amounts proposed by the Norwegian (62, 185) and Danish (186) Dietary Guidelines and the AHEI (164).

The dietary content of the scores differed depending on the available data in the surveys, but all three scores included information on coffee, tea, sugar-sweetened drinks, fruit, vegetables, potatoes, juice, fatty fish, low- and full-fat dairy products, alcohol consumption and dietary supplement use. The variables were scored between 0 and 5, with higher scores indicating a healthier diet intake. Similar food groups were scored and weighted (in relative terms) similarly in the three scores. However, owing to different content and number of dietary variables across the surveys, subvariables within food groups were potentially scored differently to achieve similar overall weights. Despite our efforts for consistency between surveys, the final scores were not identical in terms of dietary variables, number of variables

and, thus, potentially maximum achievable scores. For standardization, the participant's total score at each time point was divided by the maximum score, resulting in scores between 0 and 1 for each survey. The construction of the diet scores is described in more detail in Paper III.

3.4 Statistical analyses

Descriptive statistics were presented for the total sample and by strata of the outcome (robust versus pre-frail/frail in Paper I and robust versus pre-frail in Paper II) or exposure (dietary trajectories in Paper III). Differences between groups were tested using Student's t-test or analysis of variance for continuous variables, and chi-square test for categorical variables. Results from descriptive tests were presented as means and standard deviations or 95% confidence intervals (CIs) for continuous data, and counts and proportions for categorical data. Continuous variables were visually inspected for normality.

Tracking of dietary patterns over time was examined in different ways. In Papers I and II, stability and patterns of dietary intake were identified via cross-tabulation of tertiles of protein intake at two time points, and three levels of total fish intake at three time points, respectively. In Paper III, GBTM was used to create dietary trajectories from quintiles of three diet scores at three time points. GBTM is a form of latent class growth analysis that identifies subgroups of individuals following similar patterns of development over time for a given variable (145).

To perform meaningful statistical analyses, strata of dietary patterns or categories of intake with few participants were sometimes merged together to increase the sample size. This included 'stable low' and 'stable medium' patterns of protein intake in Paper I, which we merged to a combined 'stable low' pattern in the tracking analysis. In Paper II, the original frequency intervals of fish intake were merged to three levels of intake, similar in all surveys: low (0–3 times/month), medium (1–3 times/week) and high (≥ 4 times/week). Moreover, we expanded the conservative definition of a 'stable pattern of fish intake' from requiring three identical self-reported frequencies of intake to also allow for one out of three measured frequencies of fish intake to differ by one level of frequency.

Associations between dietary intake, or dietary tracking, and frailty were analysed using multivariable logistic regression in Papers I and II and linear regression in Paper III. The exposure variables were daily protein intake in g/kg bodyweight and g/MJ, and four patterns of stable or changing protein intake over time in Paper I, frequency of lean, fatty and total fish intake and patterns of stable total fish intake Paper II and five dietary trajectories in Paper III.

In Paper II, trends between levels of fish intake and pre-frailty were tested using the Cochran–Armitage test for trend. Effect estimates from regression analyses were presented as odds ratios (ORs) or *B*-coefficients with 95% CIs. In all papers, analyses were adjusted for baseline confounders, except for the tracking analysis in Paper II, which was adjusted for Tromsø6 (i.e. intermediate survey) confounders. Choice of adjustment variables was based on empirical knowledge on the diet–frailty relationship. In Paper I, we ran analyses with and without adjusting for energy and in Paper II, with/without adjusting for dietary supplement use. The statistical models were built according to Hosmer et al. (187), where the influence of each variable on the model's fit is assessed and reassessed until the model with the optimal fit is chosen (187, 188), relying both on statistical and empirical knowledge. If non-linearity was observed for continuous variables, these were included in their linear and non-linear forms in the models. None of the plausible biological interactions tested was statistically significant in the multivariable models.

3.4.1 Sensitivity analyses

The issue of missing data was dealt with using simple and multiple imputation (MI). In Paper I, we imputed missing outcome data to account for possible misclassification of robust participants with missing frailty data (i.e. underestimation of frailty). We manually imputed frailty (i.e. frailty score 1) in 25%, 50%, 75% and 100% of these participants, and repeated the analyses in these four hypothetical populations. In Papers II and III we applied MI for missing exposure (i.e. dietary) data at three time points. After imputation, the regression analyses were repeated and the estimates from all imputations were combined using Rubin's rule (189). In addition, in Paper III, we imputed zero in missing values of partly answered questions on intake of coffee, tea and milk in the questionnaires in Tromsø4, Tromsø5 and Tromsø7.

To address selective drop-out of participants between surveys, we compared baseline characteristics between drop-outs and re-attenders. In Paper II, we also applied inverse probability weighting (IPW) (190) and repeated the regression analysis in a hypothetical population with 100% re-attendance at follow-up, where characteristics likely lost to follow-up were up-weighted.

In Paper I, we performed sensitivity analyses to account for dominance of pre-frail/frail participants with only one frailty characteristic present in Tromsø7, and repeated analyses 1) after excluding said participants and 2) on low grip strength as outcome – as an objective

proxy for muscle function. To address potential influence of reverse causality in Paper II, we repeated the analysis on fish intake and pre-frailty 8 years later after excluding baseline pre-frail participants.

The statistical analyses in this thesis have been performed in STATA versions 16.5, 16 MP and 17. All significance tests were two sided and *P* values < 0.05 were considered statistically significant. The analyses are explained in more detail in the individual papers.

4 Summary of papers

This section briefly describes the main results from the three papers. More details are provided in the original papers.

4.1 Paper I

The aim of this paper was to analyse the association between previous (baseline, Tromsø4, 1994-95) and current (follow-up, Tromsø7, 2015-16) daily intake of protein, and patterns of protein intake over 21 years, and pre-frailty/frailty.

This study consisted of 3726 participants (51% women), with an average age of 52 years and a BMI of 25.8 kg/m^2 at baseline. At follow-up, 28% (n = 1045) were pre-frail/frail, of whom 1% were frail and 27% were pre- frail. Average total protein intake was 78 g at baseline and 93 g at follow-up, corresponding to relative protein intakes of 1.1 and 1.2 g/kg bodyweight and 17 and 18 E%, respectively, in line with the NDG (89). Overall, robust participants had a higher intake of total protein and protein in g/kg bodyweight than pre-frail/frail participants.

Results from analyses adjusted for baseline confounders and energy intake showed an inverse association between higher intake of protein intake in g/kg bodyweight and odds of pre-frailty/frailty. For 1 g/kg bodyweight increase in protein intake in Tromsø4, the odds of pre-frailty/frailty in Tromsø7 were reduced by 58% (OR = 0.42, 95% CI = 0.25,0.72). Similarly, a higher protein intake in g/kg bodyweight in Tromsø7 was associated with 49% lower odds of pre-frailty/frailty (OR = 0.51, 95% CI = 0.38,0.70). The tracking analysis showed that participants with a stable low (OR = 1.90, 95% CI = 1.16,3.09) or decreased (OR = 1.85, 95% CI = 1.14,2.99) pattern of protein intake in g/kg bodyweight over time had 90% and 85% higher odds of pre-frailty/frailty, respectively, compared with a stable high intake. Conversely, a stable high pattern of protein intake was associated with lower odds of pre-frailty/frailty compared with a stable low pattern (data not shown). No significant associations were found between intake of protein in g/MJ and pre-frailty/frailty.

These results highlight the important role of protein intake in development of pre-frailty, and thereby, the prevention of frailty. Our findings emphasize the importance of maintaining a sufficient protein intake through adulthood and into older age, as recommended by the NDG and the NNR2023.

4.2 Paper II

The overall aim of this study was to investigate the longitudinal association between fish intake and pre-frailty in Norwegian older adults.

This study included 4350 participants (52% women) with an average age of 65 years and BMI 27.2 kg/m^2 at baseline (Tromsø6, 2007–08). At follow-up (Tromsø7, 2015–16), 28% (*n* = 1124) were pre-frail. Of the participants, 37% reported a medium fish intake, corresponding to eating fish for dinner 1–3 times a week, whereas 52% had a high intake (≥ 4 times a week). Overall, the analyses showed that a more frequent fish intake was associated with lower odds of pre-frailty 8 years later (*P* value for trend < 0.05). A high intake of lean, fatty and total fish was independently associated with 28% (OR = 0.72, 95% CI = 0.53,0.97), 37% (OR = 0.63, 95% CI = 0.44,0.92) and 31% (OR = 0.69, 95% CI = 0.52,0.91) lower odds of pre-frailty after 8 years, respectively, compared with a low intake (0–3 times a month). For fatty fish, a medium intake was associated with 19% (OR = 0.81, 95% CI = 0.68,0.97) lower odds of pre-frailty compared with a low intake.

In the subsample of complete cases (*n* = 3229) included in the tracking analysis, participants with a stable high frequency of total fish intake over 21 years had 41% lower odds of pre-frailty compared with those with a stable low intake (OR = 0.59, 95% CI = 0.38,0.91). Results were similar from tracking analysis in 5750 participants after applying MI to missing fish data.

In conclusion, we showed that higher frequency of fish intake in middle-age and consistently through adulthood may reduce the odds of pre-frailty in community-dwelling older adults. This supports dietary recommendations to eat fish several times a week – both lean and fatty types.

4.3 Paper III

The overall aim of this study was to investigate the association between dietary trajectories over 21 years and frailty.

Among the 715 study participants, 55% were women and the average age was 54 years at baseline (Tromsø4, 1994) and 75 years at follow-up (Tromsø7, 2015). At follow-up, the mean frailty index score was 0.22 (range 0.4–0.54) and 31% were classified as frail.

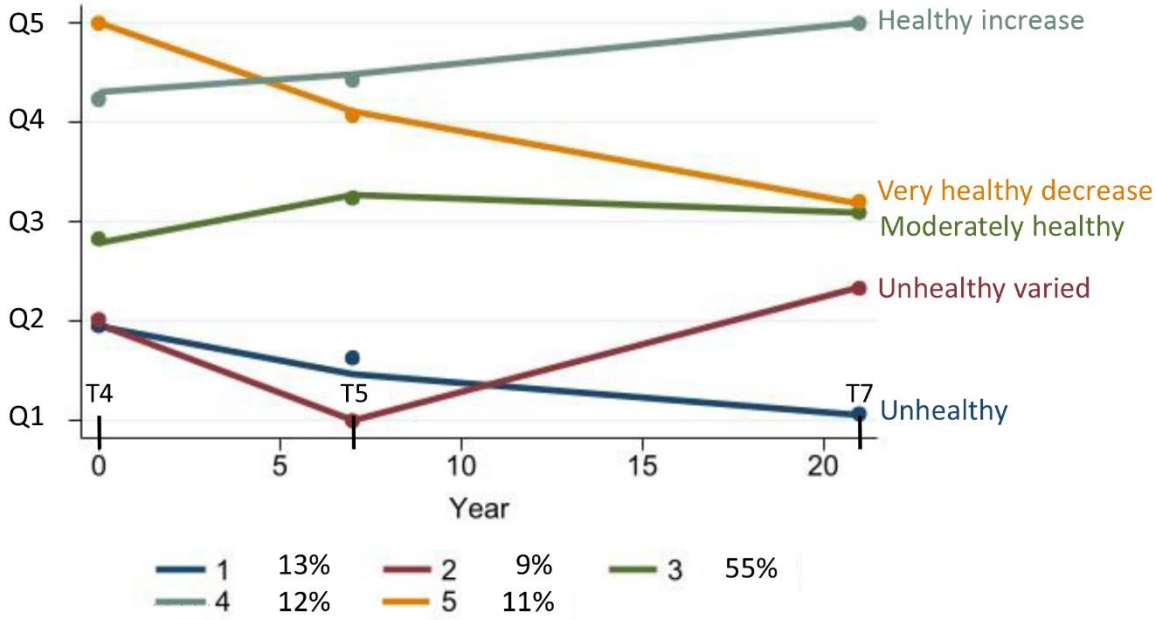

Figure 6. Dietary trajectories: unhealthy, unhealthy varied, moderately healthy, healthy increase, very healthy decrease. T4: Tromsø4 (1994–95), Q1–Q5: quintiles of diet scores, T5: Tromsø5 (2001), T7: Tromsø7 (2015–16).

Using GBTM, we identified five dietary trajectories over 21 years based on three diet scores, measuring the diet according to the NNR2023 (**Figure 6**). Of these, the trajectories 'moderately healthy' and 'healthy increase' were associated with 0.02 (β = –0.02, 95% CI = –0.04, –0.002) and 0.03 (β = –0.03, 95% CI = –0.06, –0.007) lower frailty index score at follow-up compared with the 'unhealthy' trajectory. Repeating the analysis after applying MI to missing food data (*n* = 1998), showed similar results.

To conclude, our new findings on dietary trajectories and frailty suggest that maintaining a moderately healthy to very healthy diet through adulthood is associated with lower frailty in older age. This supports the importance of encouraging a healthy lifestyle and diet already in mid-life to promote healthy ageing and prevent frailty in older age.

5 Discussion

Our results suggest that having an adequate intake of protein and fish, and eating an overall healthy diet, from mid-life onwards, may reduce the risk of pre-frailty and frailty. We believe that these findings are important contributions to the diet and frailty research field. However, we acknowledge that our studies have certain limitations and strengths, and that the results should be interpreted in the light of these. Therefore, methodological considerations will be discussed before proceeding to the discussion of results and future implications.

5.1 Methodological considerations

Like all research, epidemiological studies aim to be valid and reliable, with minimal systematic and random errors (161). According to the *Dictionary of Epidemiology*, the validity of a study refers to 'the degree to which inferences drawn from the study are valid' (191). Thus, the validity reflects how trustworthy the results are, with regard to variables and measurements (internal validity), and whether the study's results are generalizable to the population from which the study population is drawn, often the general population (external validity). Internal validity refers to the extent to which the study answers its research questions, i.e. whether or not it is free from bias (157, 191). Consequently, internal validity is largely influenced by study design, data collection, confounding and the statistical methods used.

5.1.1 Study design

This thesis is an observational, prospective cohort study based on data from four cross-sectional surveys in the Tromsø Study. Cohort studies follow a defined group of, ideally, initially healthy subjects or subjects without the disease of interest over a designated time period, to assess the effects of specific factors on the risk of disease (161). The longitudinal nature of the current study is an advantage because it allowed for repeated measures of diet and tracking of diet over time (157). Repeated measures of diet may provide additional information about the relationship assessed compared with a single measure, as repeated measures increases the likelihood of identifying changes in diet over time (i.e. after baseline) (155). Nevertheless, the observational nature of the study does not allow for claims of causality and observed relationships must be stated as associations (157).

Reverse causality

In our case, a healthy baseline population translates to participants without frailty at baseline. Baseline frailty status in Tromsø4 (in Papers I **and III** and the tracking analysis in Paper II) was not assessed due to insufficient data to define frailty. Consequently, frailty may, to some degree, already have been present before follow-up in our analyses, which potentially introduces a risk of reverse causality in the analyses. This might have influenced the observed associations and reduced the validity of these estimates. Moreover, Fried et al. originally excluded participants with Parkinson's disease, stroke and cognitive impairment and those who used antidepressant medications, because 'these conditions could potentially present with frailty characteristics as a consequence of a single disease' (40). In Paper I, data were available on stroke and antidepressant use in Tromsø4; however, none of these was set as an exclusion criterion. In Paper II, participants with MMSE scores corresponding to less-than-normal cognitive function (scores < 24) (192) in Tromsø6 were excluded, but, similar to Paper I, none of the other variables was considered as an exclusion criterion. In both papers, however, stroke was adjusted for as part of the comorbidity variable. In hindsight, we should have utilized the available data on the conditions specified by Fried and excluded participants presenting with these to minimize the risk of misclassification of frailty. Nevertheless, considering that there is 21 years between Tromsø4 and Tromsø7, we consider the risk of reverse causality from baseline frailty to be low in practice. In Paper II, whis was supported by similar results from the original analysis on fish intake in Tromsø6 and pre-frailty 8 years later and analysis after exclusion of baseline pre-frail participants.

5.1.2 Bias

In research, bias is considered to be a systematic error that causes consistent skewedness of estimates or results that reduces the validity of a study (161). As opposed to random errors, one cannot reduce the systematic errors by increasing the sample size. Study bias is largely determined by information bias, selection bias and confounding, which lead to estimates that differ systematically from the truth (157).

Information bias

Information bias, also known as measurement bias, occurs when the information recorded in a study is flawed (157). In particular, information bias is linked to self-reported data, which is prone to recall error and social desirability bias when individuals (intentionally or not) answer in a certain way to represent themselves in a more favourable light (160, 193, 194). A major

limitation of the current thesis is that most of the variables investigated were self-reported by the participants through questionnaires. Overall, the presence of measurement errors in exposure, adjustment variables and outcome may lead to bias in both directions – i.e. underestimation or overestimation of effect estimates (161).

Selection bias

Selection bias may be defined as 'an error introduced when the study population does not represent the population intended to be analysed' (157). As seen in population studies in general (195), Vo et al. showed that Tromsø7 participants were more highly educated and of higher socioeconomic status than non-attenders (196). This was reflected by the overall relatively good health and few comorbidities among the study participants in the present thesis, and that those who attended several of the Tromsø surveys were healthier and had better socioeconomic status than those who attended only at baseline (**Supplementary Table S4**, Paper I). The latter showed that the sample suffered from attrition bias, a type of selection bias that is caused by selective drop-out of participants with specific characteristics between surveys. Bias introduced by differences between participants and non-attenders is challenging to overcome because participation is voluntary, and especially when participation is not reimbursed.

One statistical method to handle selective drop-out is by IPW (190), which we applied in Paper II. Contrary to the main results in paper II, the analysis performed in the hypothetical, more heterogeneous study sample created with IPW showed no associations between fish intake and pre-frailty. This suggested that the study sample in paper II suffered noticeably from selection bias, and thus the results should be interpreted with caution. One may speculate that, in the IPW sample, the effects of age and poorer health superseded the positive effects of frequent fish intake observed in the original study population. It would have been interesting to also apply IPW in the other papers; however, in Paper I, I was not familiar with IPW and, in Paper III, we prioritized to apply MI for missing food data, including in participants originally excluded from the analysis, which significantly increased the sample size and thus provided a somewhat less restricted sample.

Overall, non-attendance by the frailest individuals in the Tromsø Study will have contributed to underestimation of frailty in the study sample in Papers I and II, which may have influenced the observed associations. Similarly, non-attendance by individuals with the least healthy diets may have contributed to an overestimation of the effect of diet on frailty risk, as

indicated by the results from the IPW analysis in Paper II. Consequently, the presence of selection bias might have reduced the study's internal validity.

Confounding

Confounding is an inherent problem of epidemiological studies. A confounder is a variable that influences the association between the exposure and the outcome because the confounding variable is, in itself, associated with both the exposure and the outcome (197). The effects of confounding may be reduced through applying multivariable statistical models, where confounding variables are adjusted for, allowing for the estimation of the specific effect of the exposure variables (197). Notably, observational studies inevitably suffer from residual confounding, i.e. confounding from unmeasured or not properly measured factors, which cannot be solved statistically (157). In this thesis, we performed multivariable regression models, adjusting for baseline confounders known to be associated with diet and frailty. Statistical adjustments to handle confounding are be discussed in more detail under 5.1.3 'Statistical considerations'.

5.1.3 Dietary data

Validity of data

There are no validation studies on the dietary data obtained from Tromsø4–Tromsø6. However, the estimated E% from macronutrients in Tromsø4 were comparable with data from Norkost 1 (1993–94) and 2 (1997), which were supposed to be the most representative sample of the general Norwegian population aged between 16 and 79 years, at the time (90, 91), suggesting that the estimated dietary intakes are reasonably reliable. The FFQ used in Tromsø7 had been validated against weighted food records and plasma biomarkers and considered suitable to assess total diet in large population-based surveys (198, 199); however, one study did find that the estimated E% from fat and sugar was slightly underestimated, while the E% from carbohydrates and protein was slightly overestimated (199). Under-reporting of certain foods and consequently underestimation of nutrient intake may lead to attenuated effect estimates, and conversely, overestimation of nutrient intake may lead to amplified effect estimates (199).

Comparability of dietary data

A major challenge in the planning and analyses of the studies conducted was that the collected dietary data differed between the Tromsø surveys, which hampered direct comparison of the dietary items. Despite our efforts to compare repeated measures of similar

dietary items, the dietary variables registered and analysed were not always identical. This restricted our options as to which dietary variables, and how many measurements of these, we could investigate.

In paper I, the estimated protein intake in Tromsø4 was based on 34 food-related questions with portion sizes estimated based on previous dietary surveys, whereas estimated intake in Tromsø7 was based on a 261-item FFQ specifically asking about portion sizes. Consequently, the consistently observed higher estimated protein intake in Tromsø7 may reflect that the protein estimates in Tromsø7 were based on a much higher number of dietary variables than that in Tromsø4 and that participants were more inclined to report consumption of the foods and beverages when specifically asked about these. Moreover, the observed differences in protein intake is likely to also be attributed to the observed overestimation of protein E% from the FFQ used in Tromsø7 (199).

In paper II, the questions about fish intake in Tromsø4 and Tromsø6 asked about frequency of intake of lean and fatty fish *for dinner*, whereas meal type was not specified in Tromsø7 (overview of original questions in **Supplementary Table S1**, paper II). Thus, although handled and analysed as identical variables, one may speculate that the participants may have reported a higher fish intake to the questions *not* restricted to fish dinners. If so, this may suggest that fish intake in Tromsø7 was relatively over reported compared to the fish intake in Tromsø4 and Tromsø6, which could explain that the observed fish intake was highest overall in Tromsø7. Notably, only fish intake in Tromsø6 was analysed individually, however, this possible difference in self-reported intake may have influenced the identified patterns of fish intake, which included all three surveys.

The issue of differing dietary data in the Tromsø Study surveys had the most consequences for the analysis in Paper III, which included the greatest number of dietary variables. The dietary trajectories were based on three different diet scores of the participants' diets, based on different sets of available dietary variables at each time point and thus, not directly comparable. As the diet scores for Tromsø4 and Tromsø5 did not cover the total diet, these scores were proxies for total diet scores. The trajectories showed patterns among the participants with higher or lower diet scores over time, *relative to each other* and consequently, the trajectories merely ranked the participants' relative diet scores over time. Overall, although the diet scores themselves cannot be directly interpreted as a measure on a healthy diet, we believe that the trajectories – the exposure in Paper III – may be interpreted

as relative measures of different levels of a healthy long-term diet, and applied to other relatively healthy adult and older adult populations and thus, considered externally valid.

Construction of diet scores

A major methodological concern with regard to construction of diet scores is researcher subjectivity (126). For example, subjective decisions are made regarding what dietary items are relevant to analyse, how to define different food groups and how to score different food variables. Although the NNR2023 provided the basis for the diet scores in Paper III, with specific recommendations for intake of most of the nutrients and foods, we constantly had to make subjective assessments of the recommendations against the dietary variables in the Tromsø Study when constructing the diet scores. The process was complicated by the different available dietary variables in the three surveys, meaning that similar dietary recommendations was sometimes interpreted and measured in three different ways. Nevertheless, as far as possible, the structure and scoring systems were similar in the three scores, with healthy variables receiving higher scores, and similar variables scored similarly, and thus weighted – relatively – equally in each survey.

Both the contents of FFQs and people's dietary habits are influenced by the times in which we live, including trends, recommendations and beliefs in diet and health. Thus, it may be debated whether the use of dietary recommendations from 2023 is an appropriate measure of diet measured in 1994, 2001 and 2015, respectively. Moreover, the NNR was not targeted towards the study population in Paper III, but towards the general population of 2023, encompassing all age groups and individuals with and without diseases (63). However, we argue that it was a suitable choice, considering the following: first, with the exception of Tromsø7, the available dietary data in the Tromsø Study were not sufficient to measure adherence to neither current nor previous national dietary guidelines. Second, the NNR2023 is the most comprehensive dietary guideline available, which makes it possible to assess far more variables from the Tromsø Study dataset than any other existing dietary guidelines or diet scores. Third, we believe that what is recommended today would also have been recommended in the 1990's – if one had had the knowledge at the time. Fourth, in Paper III, we did not measure *adherence to dietary guidelines*, but we tried to measure an objectively healthy diet, based on available data.

5.1.4 Frailty data

The frailty definitions used in this thesis were based on an overweight of self-reported data, which introduce a higher risk of information bias than if they had been objectively measured.

When defining physical frailty according to Fried et al. (40), the characteristics should ideally be measured similarly to the original operationalization. However, most studies – as much as 90% according to a systematic review (55) – use study-specific modified versions of the definition. Also in Papers I and II, four of the five frailty characteristics measured in Tromsø7 were slightly modified from the original physical frailty definition, because these were measured with different instruments, as presented in Table 2, and in detail in Supplementary Table S1, Paper I. According to the aforementioned systematic review, the modifications used in Tromsø7 for the different characteristics, were among the most common modifications (55), and the measurement instruments used in Tromsø7 were well known and validated, which indicates that physical frailty in Tromsø7 was measured using an acceptable definition.

One drawback of Papers I and II was that the pre-frail/frail and pre-frail groups were heavily dominated (> 80%) by participants with only one frailty characteristic present. Furthermore, among these participants, about half had self-reported low physical activity as the only frailty characteristic present. We argue that this reflects how Fried's frailty definition may not have been sensitive enough, or an unsuitable measure for this population, considering that we, to some extent – in essence – analysed the association between diet and low physical activity. All analyses were adjusted for baseline physical activity, which to some extent handled the issue of possible reverse causality caused by inactive participants at both baseline and follow-up. Notably, results from sensitivity analyses performed in Paper I, in an attempt to overcome the dominance of those with only one frailty characteristics, where we 1) excluded participants with frailty score 1 and 2) ran the analyses on the objectively measured low grip strength as a proxy for muscle function, were similar to the study's main finding.

Regarding the frailty index in Paper III, we consider it to be an overall robust definition of frailty when handled as a continuous variable as it was constructed according to an objective formula and covered several different aspects of health (51).

5.1.5 Statistical considerations

In the following section, we outline the statistical methods used in this thesis, and their suitability, if not already discussed above.

Statistical adjustments

In the papers in this thesis, the statistical models were adjusted for baseline variables – measured 21 years (Papers I and III) and 8 years (Paper II) before follow-up. We acknowledge that 21 years is a very long time period and that all characteristics measured at baseline will not necessarily be applicable at follow-up. To account for this, in Paper I, we also performed analyses that were adjusted for follow-up confounders, which gave similar results as those adjusted for baseline confounders.

For the papers with three time points, we considered the possibility of performing mixed model analyses, and thereby accounting for the effect of time by adjusting for time-varying confounders, however this was not possible owing to the nature of the data as mixed models are only applicable to repeated measurements of *outcome* – not exposure.

In Paper II and III, some baseline adjustment variables were also included in the outcome which could possibly have contributed to over-adjustment. For example, in Paper II, the analyses were adjusted for Tromsø6 (baseline) physical activity level, 8 years before follow-up. This variable was statistically significant in univariate and multivariate analyses in the model-building process and, more importantly, the statistical fit of the model was higher with physical activity included the model than without. Also, adjusting for baseline physical activity might, to some extent, have accounted for a possible risk of reverse causality introduced by the high levels of pre-frail participants at follow-up which had low physical activity as their only frailty characteristic present (51%) (**Supplementary TableS9**, Paper II). The results did not change notably depending on the variable physical activity was in the model or not (data not shown). Combined, we therefore believe we had solid grounds for including physical activity in the statistical models and that the risk of over-adjustment appeared low. In Paper III, the adjustment baseline variables BMI, self-reported health and social status were also included in the frailty index. However, we consider the 21 years between assessment of these baseline variables to follow-up and construction of the frailty index as sufficient for this not to pose a statistical problem.

We were consistently interested in the diet–frailty effects in men and women separately, because sex is strongly associated with frailty and dietary habits differs between the sexes

(200). However, for most of the analyses – including all tracking analyses – the strata-specific sample sizes were once again too small and, thus, we did not perform sex-stratified analyses.

Moreover, we acknowledge that reporting changes in 'risk' of pre-frailty/frailty in Paper I was inaccurate because ORs should be interpreted as risk ratios only if the outcome is rare (< 10%), or it will otherwise overestimate the risk (197).

Adjusting for dietary variables

In dietary research, it is often recommended to adjust for energy intake (161). When energy intake is associated with the outcome, it acts as a confounder because the intake of most nutrients is (strongly) linked with energy intake. Also, when not associated with the outcome, variations in energy intake may lead to variations in nutrient intake as a result of individual differences in physical activity, body size and metabolism. Failing to adjust for energy intake may lead to an underestimation of associations (201). In this thesis, only the analyses in Paper I were energy adjusted. In Paper II, baseline energy intake was not adjusted for as no such data was available. Consequently, the observed association between fish and pre-frailty may be overestimated, if some of this is truly attributed to energy intake. In Paper III, because all macronutrients in the diet scores were included as E%, we considered that adjusting for energy intake would have led to over-adjustment.

Moreover, it would have been fruitful to perform substitution-analyses, to assess the effect of the nutrient or food in focus, depending on the additional composition of the diet. For example, in Paper II, it would have been interesting to see the effect of eating fish *instead* of other relevant foods (e.g. meat, vegetables, snacks); however, no such analyses were done owing to insufficient data.

In Paper I, protein intake in g/kg bodyweight/day was analysed in units of 1 g/kg bodyweight/day, which arguably is too large a scale for any meaningful interpretation. Our results showed that for every 1 g of increased protein intake per kg bodyweight, the odds of pre-frailty reduced by 57%. However, this is an unrealistically large change, considering that the average intake in the study participants was about 1.1 g/kg bodyweight/day and that the NNR2023 recommend daily protein intakes of 1.2–1.5 g/kg bodyweight for older adults (63). A more suitable unit might have been 0.1 g/kg bodyweight/day, which represents a more realistic change in protein intake in everyday life.

Tracking analyses

Several pragmatic decisions were made regarding the identified dietary patterns for facilitating meaningful statistical analyses of these. For clarity, although consistently labelled as 'tracking analyses', this term is really only suitable for Papers I and II, which focused on *stable* and *changing* dietary patterns of intake. However, Paper III focused on dietary *trajectories*, which do not concern stability of intake specifically, but rather varying and complex patterns of intake over time.

In particular, the results from the tracking analysis in Paper II must be interpreted with caution because the 'stable' patterns of fish intake in practice may vary significantly within the categories, considering that the definition of the stable patterns allowed that one out of three measured frequencies of fish intake could differ from the other two. Thus, similarly classified stable patterns of fish intake may in reality vary a great deal, depending on whether the pattern consisted of three or two identical measures, whether the 'one-off' intake frequency was higher or lower than the other two and, if so, in what survey.

In contrast to in Papers I and II, the dietary trajectories in Paper III were created statistically using GBTM. As a data-driven method, GBTM inhibits a low risk of researcher subjectivity because the identified patterns are not chosen by the researcher. However, the researcher must still make certain assessments during the construction of the final model by comparing the suitability of different models with different numbers and shapes of included trajectories. Unlike previous longitudinal analysis methods that tend to describe trends in dietary intakes or behaviours as a group average over time, GBTM accounts for between-individual variation and recognizes subgroups of individuals who present with distinct patterns that vary from the group average (142). Overall, we believe that the GBTM was a suitable choice of method for identifying the dietary trajectories. However, it is worth remembering that the identified trajectories include participants with various combinations of diet scores over time and that the final trajectories (**Figure 6**) represent their average diet scores. For example, at each time point there were some participants with diet scores in the highest and lowest quintiles who nevertheless were included in the 'moderately healthy' trajectories, based on their diet scores at the other time points. Thus, the dietary trajectories must be interpreted at a population level and not at the individual level.

Handling of missing data

Missing exposure data

In Papers II and III, missing dietary data were imputed using MI. MI is a flexible, simulation-based statistical method for handling missing data, allowing for the uncertainty of the missing data by creating multiple, different, plausible, imputed datasets and appropriately combining the results from each of these (202, 203). Consequently, the multiple datasets in MI reflect the variability in the study population to a greater degree than achieved with simpler imputation methods, which increase the reliability of inferences drawn from MI analyses. MI is suitable when data are assumed to be missing at random (MAR). If missing data are MAR, it depends on observed values and, therefore, we assume that we can predict the missing values based on the other observed data (197). Thus, we believe that using MI was a suitable choice to impute the missing dietary data.

In addition, simple (zero) imputation was applied for selected dietary variables in Paper III. Although zero imputation is a common, simple method of dealing with item non-response in FFQs, it makes strong assumptions about the missing data mechanisms and disregards any uncertainty about the true value to impute and, therefore, it is not an appropriate imputation strategy for all missing FFQ items – as opposed to MI (204, 205). Nevertheless, we considered it an acceptable imputation method for the selected, partially answered, dietary questions where we considered that the lack of response was likely due to an actual null value.

Missing outcome data

In Paper I, but not in Paper II, we excluded participants with missing data on three or more frailty characteristics in Tromsø7. In Paper II, we considered this exclusion criterion as unduly strict considering that the outcome assessed (pre-frailty) required the presence of 'only' one frailty characteristic. In retrospect, I believe that we should have applied said exclusion criterion for consistency between the studies and to reduce the degree of missing data. However, exclusion of participants with three or more missing frailty data in Paper II (data not shown) had no influence on the observed pre-frailty prevalence.

Furthermore, we only imputed missing outcome data in Paper I. The chosen imputation method was arguably a suboptimal choice, considering that it was not validated and was very monotonous because it consistently imputed '1' frailty score for the missing frailty data, which is unlikely to reflect the reality. At the same time, this imputation method did most

probably introduced little risk of researcher subjectivity as there were no variations or room for interpretation of the imputed values. The results from the analyses performed after imputing frailty were in line with the study's main results, suggesting that the risk of underestimation of frailty due to missing data was low.

We could also have imputed outcome in Paper II, considering that 35% of the participants had missing frailty data. However, I suspect that the prevalence of frailty would not have changed drastically after imputation because I believe that the observed low frailty prevalence is the result of selection bias and not missing frailty data. In Paper III, only ten participants were excluded based on missing frailty data and only one variable was deleted from the index because > 10% of the participants had missing data.

Bearing the described considerations, restrictions and errors outlined in mind, we believe that overall, the statistical methods used were suitable choices for analyses of the diet-pre-frailty/frailty associations. In addition, the increasingly complex statistical methods used in Papers I–III reflect my progression in statistical skills.

In summary, despite the outlined presence of selection bias, information bias and risk of residual and/or unmeasured confounding in the studies, all of which reduce the studies' internal validity, we consider the observed estimates from the statistical analyses performed – consistently supported by the results from sensitivity and supplementary analyses – suggesting that the results have, in general, an acceptable internal validity. Thus, given the discussed limitations and that the results are interpreted with caution, we believe that our findings may be generalized to relatively healthy community-dwelling adults and older adults in Norway and comparable populations.

5.2 Discussion of the main results

The studies in this thesis investigated the association between a nutrient (Paper I), a food group (Paper II) and an overall diet (Paper III) and frailty.

The main findings of this thesis were that a higher daily protein intake in g/kg bodyweight in middle age was associated with lower odds of pre-frailty/frailty in older age (Paper I). Similarly, a frequent intake of fatty, lean and total fish was associated with lower odds of pre-frailty 8 years later in older adults (Paper II). Moreover, through analyses on dietary tracking over 21 years, we showed that maintaining a consistent high protein intake (in g/kg bodyweight/day) (Paper I), a frequent fish intake (Paper II) or a moderately healthy to very

healthy diet (Paper III), from middle-age onwards, was associated with lower pre-frailty/frailty in older age. As far as we are aware, our studies are the first to investigate the longitudinal association between dietary tracking and pre-frailty/frailty.

These findings support the hypothesis that diet in adulthood influences the health in older age, and therefore, that maintaining healthy dietary habits throughout life is crucial. This thesis adds valuable findings to diet–frailty literature and, in particular, the results from dietary tracking analyses contribute with new findings to an area of research where there is a consistent demand for more longitudinal studies.

In the following section, the results and implications from the three papers included in this thesis are discussed in the light of existing research.

5.2.1 Associations between diet and frailty

Protein intake and pre-frailty/frailty

In Paper I, we showed that higher protein intake in g/kg bodyweight/day, and maintaining a stable high level of intake over time were associated with a lower odds of pre-frailty/frailty in older age. We found no statistically significant associations between protein in g/MJ/day and pre-frailty/frailty.

Results from two longitudinal studies in community-dwelling older women are in line with our findings of an inverse association between higher protein intake in g/kg bodyweight and frailty/pre-frailty (99, 100). In a 3-year Finnish cohort, Isanejad et al. found that women with protein intake ≥ 1.1 g/kg bodyweight had lower odds of physical frailty, compared with those consuming < 1.1 g/kg bodyweight (99). Similarly, Vellas et al. reported that women aged ≥ 60 years with a daily protein intake > 1.2 g/kg bodyweight had fewer health problems and less (study-specific) frailty after 10 years compared with those consuming < 0.8 g/kg/day (100). Also, in line with our findings, the results from the Newcastle 85+ study showed that increased intake of protein in g/kg bodyweight adjusted to normal BMI decreased the likelihood of worsening frailty status over 5 years in men and women aged ≥ 85 years (101). On the contrary, however, a 16-year cohort study in Dutch men and women aged ≥ 45 years found no association between daily protein intakes of > 1.2 g/kg bodyweight and < 0.8 g/kg bodyweight, and physical frailty (67). Notably the participants in the latter two studies were very old and middle-aged, respectively, and therefore might not be directly comparable with our study population. Results from cross-sectional studies on protein intake in g/kg

bodyweight and physical frailty in community-dwelling older adults are inconclusive, with reports of both inverse associations (106) and no association (105).

The observed null-findings between protein intake in g/MJ/day and pre-frailty/frailty was somewhat surprising, especially considering the consistently observed inverse association for protein in g/kg bodyweight/day. For results on protein in g/MJ/day, comparison are made with studies on protein E%. In line with our findings, are findings from Shikany et al. who found no association between quartiles of protein E% and physical frailty over 4.6 years, in US older men (70). Moreover, among community-dwelling Norwegian adults, Sabir et al. found no association between substituting 1 E% protein with carbohydrate or fat in middle age (46–49 years) and appendicular skeletal muscle mass or grip strength in older age (67–70 years) (103). Contrary to this, a Japanese and a Norwegian cross-sectional study found an inverse association between protein E% and frailty (104) or walking speed (107) in community-dwelling older adults, respectively.

To the best of our knowledge, only one previous study – Beasley et al. from 2010 – has analysed the association between protein intake assessed relative to both bodyweight and energy intake and frailty (98). Notably, their findings differed from ours in that they observed an inverse association between higher intake of both protein parameters and pre-frailty/frailty, whereas we saw only an association for protein intake in g/kg bodyweight. Beasley et al. reported that, in 24 417 women in the Women's Health Initiative cohort, a 20% increase in protein intake in g/kg bodyweight/day and protein intake in E% over 3 years was associated with 35% and 32% lower odds of physical frailty, respectively. For pre-frailty, 22% and 24% lower odds were observed (98). The authors observed attenuated associations between total protein intake (g/d) and frailty, to which they commented that 'the nutrient density estimates of protein intake (E%) are consistently more predictive of health outcomes than absolute estimates of protein intake (g)'.

Although the two protein parameters assessed in Paper I reflect different aspects of protein intake – relative to both body size and energy intake (i.e. as a proportion of the total diet), we hypothesized that their observed association with pre-frailty/frailty would be somewhat similar, or in the same direction. However, the two protein variables had poor correlation (data not shown), showing that they truly measure different aspects of diet. Moreover, we speculate that the different observed estimates might be partly explained methodologically by the different inherent sources of error in the denominators of the two variables, that is the

objectively measured bodyweight versus estimated energy intake based on self-reported dietary data. In addition, the observed association for protein in g/kg bodyweight might somehow reflect differences in body composition between groups, considering that the pre-frail/frail participants on average had slightly higher bodyweight than the robust participants. However, this was not investigated further owing to a lack of body composition data.

Research is inconclusive on the influence of animal versus plant protein sources (67, 69, 71, 206, 207), the distribution of protein intake across daily meals (105, 107, 208), and the effect of protein supplementation on risk of frailty (209). These aspects of protein intakes were, however, not investigated in Paper III owing to lack of data.

The protein intake in the highest tertile was in line with the NNR2023 at both baseline (≥ 1.2 g/kg bodyweight) and follow-up (≥ 1.4 g/kg bodyweight) (63). Thus, our findings of higher odds of pre-frailty/frailty from long-term protein intakes below these levels, and conversely, lower odds of pre-frailty/frailty from consistent intakes at these high levels, may indicate that having a long-term protein intake in line with, or even higher than the dietary recommendations may be associated with lower odds of pre-frailty/frailty in older age.

The protein intake in Norway is generally high, and most people get enough protein through their normal diet. Thus, our findings do not imply that the Norwegian population as a whole should increase their protein intake unrestricted. However, our findings emphasize the importance of maintaining a high protein intake with increasing age. This is especially important for vulnerable groups at risk of insufficient protein intake, such as adults and older adults who are lonely, suffer from diseases or dental health issues, or have poor appetite. In addition, vegetarians and vegans must make sure that they get enough protein in their daily diet, which can be a challenge because protein from animal sources is generally of a higher quality and more efficiently utilized by humans, compared with plant proteins (61). Sources of plant proteins include pulses (e.g. beans, lentils and peas), nuts, seeds, whole grains and soy products. With the exception of whole grain (bread), these are foods that are consumed to a low extent in Norway (210), but – at a population level – we could benefit from eating more of them, from both a health and a climate perspective. This is reflected in the NDG and NNR2023, which both emphasize that legumes, nuts, seeds and whole grains should be a significant part of a healthy diet (62, 63).

Increased knowledge about dietary sources of protein, including plant protein, and what constitutes a well-balanced diet and thus a diet with sufficient protein content, will be useful

for the general Norwegian population, but especially those with low *nutrition literacy* ('the degree to which individuals have the capacity to obtain, process, and understand nutrition information and skills needed in order to make appropriate nutrition decisions' (211), and those who eat too little protein. Moreover, this knowledge is important for relatives and health workers who are involved in cooking and/or serving, to be able to suggest and offer good and appropriate food choices.

Fish intake and pre-frailty

In Paper II, we observed that a high intake (≥ 4 times/week) of fatty, lean and total fish was associated with lower odds of pre-frailty after 8 years compared with a low (0–3 times/month) intake in Norwegian older adults. For fatty fish, a medium intake (1–3 times/week) was also associated with lower pre-frailty 8 years later. Moreover, maintaining a stable high intake of total fish over 21 years was associated with lower odds of pre-frailty compared with a stable low intake over time.

As the existing literature on fish intake and *pre-frailty* is limited, the comparison of our results is mostly restricted to studies on frailty or frailty-related parameters, including studies with different frailty definitions and measurements of fish intake, and study populations markedly different from the relatively healthy community-dwelling older Tromsø residents that participated in Paper II. Furthermore, as we know of no previous studies on patterns of fish intake over time, we have not been able to compare the results from the tracking analysis with existing literature.

However, in line with our findings of lower odds of pre-frailty among frequent fish eaters, results from a recently published longitudinal study in community-dwelling Korean adults aged ≥ 70 years showed that fish intake was associated with lower odds of physical frailty after 4 years (212). Moreover, García-Esquinas et al. found that higher daily consumption of total fish and 'blue' (mostly fatty) fish was associated with a lower accumulation of age-related health deficits after 6 years in Spanish community-dwelling adults aged ≥ 60 years (121). However, contrary to our findings, they found no association between intake of white (mostly lean) fish and accumulation of health deficits.

Somewhat in line with our findings on fatty fish, Del Brutto et al. reported a stepwise decrease in frailty scores per additional weekly serving of fatty fish among participants aged 60–69 years, but not among those aged ≥ 70 years, in a cross-sectional study conducted in rural Ecuador (124). Among the latter, the authors suspected that the detrimental effects of

age superseded the observed positive effects of fatty fish. Furthermore, fatty fish consumption was associated with increased grip strength in men and women aged 59–73 years in the Hertfordshire cohort study (125).

In addition, Japanese (123, 213, 214) and Irish (122) cross-sectional studies have found inverse associations between fish intake and frailty. Shibasaki et al. showed that fish consumption (≤2/week) was associated with higher prevalence of pre-frailty and frailty, defined using a Japanese, internationally validated definition of frailty in older community-dwelling women, compared with daily consumption (214). Using the same frailty definition, Yamaguchi et al. reported lower prevalence of frailty among older community-dwelling adults with higher quartiles of seafood intake (213). In another study in middle-aged Japanese women with rheumatoid arthritis, the prevalence of pre-frailty and frailty was significantly lower among those who ate fish ≥ 3 times/week (123). Similarly, higher intake of total fish was significantly associated with lower prevalence of Fried's frailty in Irish community-dwelling older adults (122) and improved walking speed in older Norwegian women (107).

Also, in support of the beneficial effect of a frequent intake of lean fish observed in Paper II, results from a 10-week Saudi-Arabian intervention study showed that eating lean fish twice weekly was significantly associated with increased muscle mass and function among 22 adults aged ≥ 50 years (120).

The observed fish intake in Paper II was generally very high, with > 50% eating fish ≥ 4 times per week and 13% eating fish daily or more often. One might speculate that fish intake could be over-reported due to social desirability considering the role of fish as a healthy food (215), however, this is more applicable to younger generations than to older ones – such as the study participants in Paper II – where fish has to a greater extent been an everyday part of the diet for all social classes, and less connected to status or health (118). Moreover, the observed fish intake was in line with that among adults living in Northern Norway found in the Norkost 3 survey, which was much higher than in the rest of the country (92).

With the exception of fatty fish, our analyses showed that having a high (≥ 4 times/week) but not a medium (1–3 times/week) intake of lean and total fish was associated with lower odds of pre-frailty. Although not entirely comparable, the medium frequency category resembles the Norwegian recommendations of eating fish 2–3 times/ week (116). We were somewhat surprised by the null findings for medium lean and total fish intake, because we hypothesized that this level of fish intake would also be markedly healthier than a low intake (≤3

times/month). Taking into consideration the somewhat stronger associations for fatty fish, one could speculate that it was the main driver for the observed association between total fish and pre-frailty. Moreover, the difference in the observed associations for fatty and lean fish might reflect biological differences between the two, with fatty fish containing more anti-inflammatory LCn-3FAs and vitamin D, crucial for bones and muscles (63). However, we cannot say with certainty what caused the observed differences, just as we cannot say anything about whether there were other not known and not measured confounding factors among the participants who ate fish or in their lifestyle that influenced the associations. We also do not know what those who ate little fish ate instead and vice versa.

In Paper II, the tracking analysis showed that maintaining a stable high intake of total fish over 21 years was associated with a lower odds of pre-frailty compared with a stable low intake over time. As noted, these results should be interpreted cautiously given that the 'stable patterns' may vary somewhat. However, as a truly stable pattern of fish intake corresponds to eating fish ≥4 times/week for two decades, our findings suggest beneficial health effects from a long-term fish intake that exceeds the NDG and NNR2023 (63, 116). The results in Paper II add to those of Paper I, because total fish intake was highest in the highest tertile of protein intake (g/day) in both Tromsø4 and Tromsø7 – the two surveys with data on estimated protein intake (data not shown). In addition, the protein intake differed significantly between participants with different levels of fish intake, and increased with higher levels of fish intake (data not shown).

Our findings emphasize the importance of eating fish, and in particular, fatty fish, several times a week. As the overall fish consumption in Norway is gradually declining, particularly among younger people, promotion of increased fish intake should be prioritized. It is important to break down barriers related to fish, especially among the younger generation. This includes: spreading knowledge about the unique and healthy nutritional content of fish; how to, easily and realistically, prepare and use different types of fish and seafood; pricing fish reasonably and break down the prejudice that fish is expensive, such as the campaign 'Fish Tuesday' in the *Meny* and *Coop Mega* supermarkets in Norway, with a 30% discount on all fish products every Tuesday; and increasing the availability and selection of fish in the stores and develop more, varied and appealing fish products that can be eaten for breakfast, lunch and dinner (118). An increase in the intake of fish at the expense of meat is also favourable from a climate perspective.

Notably, adjusting for the use of cod liver oil, vitamin D or LCn-3FA dietary supplements did not influence the observed association between fish intake and pre-frailty. This indicates that it is the fish itself, or the action of eating fish – possibly at the expense of something specific else – that is associated with a reduced odds of pre-frailty.

Dietary trajectories and frailty

In Paper III, we identified five dietary trajectories over 21 years, based on the NNR2023. Of these, the trajectories 'moderately healthy' and 'healthy increase' were associated with lower frailty in older age, compared with the 'unhealthy' trajectory.

As there are no previous studies on dietary trajectories and frailty, comparison with other studies is limited to studies on dietary trajectories and health-related outcomes and mortality, in addition to studies on diet measured at a single point in time and frailty in older adults. Moreover, the inclusion of younger study populations, varying follow-up periods and study-specific dietary trajectories hampers comparison even further.

The results from longitudinal studies are somewhat in line with our findings in Paper III, showing positive effects from trajectories that reflect improved or maintenance of stable high adherence to different definitions of healthy diets over time on health outcomes – all of which were covered in the frailty index.

Findings from the Baltimore Longitudinal Study of Ageing investigating adherence to the AHEI in participants aged 30–59 years showed that participants with a 'greatly improved' trajectory had better physical function at age ≥ 60 years than those with a 'moderately improved' trajectory (146). Moreover, two Chinese longitudinal studies reported better cognitive performance (151, 152) and lower risk of poor psychological and social health (151) at older ages among participants with 'stable high' adherence to the Dietary Approach to Stop Hypertension (DASH) diet for 23 years (151) and to the AHEI for 6 years (152), respectively. Several studies have investigated the association between dietary trajectories and cardio metabolic outcomes in Chinese (148-150) and British (147) adults. Three studies investigated the association using *a posteriori* identified dietary patterns, showing overall that adherence to the healthier study-specific dietary patterns over time was inversely associated with BMI and waist circumference (147, 150) and glycated haemoglobin and diabetes (149).

Similarly, results from the Chinese Health and Nutrition Survey showed that in adults aged ≥ 18 years, changing from a relatively low-fat/high-carbohydrate diet to a high-fat/low-carbohydrate diet over 20 years was positively associated with obesity, diabetes and mortality

(148). This is in line with the NNR2023, which recommends a higher proportion of carbohydrates than fat in the adult diet (45–60 E% versus 25–40 E%) (63).

Another study from the Chinese Health and Nutrition Survey found lower total mortality among participants with improved and moderate-to-high adherence to the Chinese Healthy Eating Index over 9 years (153). Similarly, in 48 000 US women and 26 000 men, Sotos-Prietro et al. reported a lower total mortality among participants with improved or stable high adherence to three diet quality scores (AHEI, Alternate Mediterranean Diet Score and DASH) over 12 years (154).

Taken together, the above results show that it is not necessarily one specific diet that promotes good health in older age, but that different diets containing essential healthy components are associated with better health outcomes over time. Despite cultural differences and many Chinese studies, the diets included in the discussed studies – and in particular the *a priori* defined ones – were overall in line with the NNR2023, as they were rich in whole grains, fruit and vegetables, dairy, fish, and polyunsaturated fats, with less meat, sugary and fatty foods (63).

Moreover, our findings in Paper III are supported by longitudinal studies on dietary patterns and frailty, measured using the frailty index. Overall, studies agreed that adhering to healthy diets (e.g. the Mediterranean diet, the Dutch Dietary Guidelines and Diet Quality Index–International) were associated with a lower risk of frailty (128, 129, 216, 217), slower progression of frailty (129) and increased likelihood of study-specific definitions of healthy ageing (135, 218).

As the first of its kind, we believe that our study contributes with important new findings on the association between diet and frailty from a longitudinal perspective. Our results show a positive effect of a consistently moderate or (very) healthy diet from adulthood to older age. Even if a diet classified as ‘very healthy’ is based on higher diet scores, indicating an objectively healthier diet than a ‘moderately healthy’ diet, the trajectories are similar in that they do not reflect decreasing diet scores but conversely, similar or increasing diet scores over time. In other words, our results also show a protective effect of simply avoiding worsening dietary habits with age. We cannot specify how the participants in the different dietary trajectories ate over time, as only the diet score in Tromsø7 covered the whole diet and their contents vary. However, in general, a healthy dietary pattern, more or less in line with the dietary recommendations, is assumed to provide both a certain intake of foods and nutrients

that should cover the body's primary needs and the prerequisites for generally good health and a lower risk of diet-related diseases (62, 63). Thus, our results may be interpreted as individuals who more than others ate a diet in line with the NNR2023 over time, defined based on varying available data at each point in time, were less frail than those whose diet deviated more from the recommendations. Overall, this emphasizes the importance of eating a varied and healthy diet and adhering to dietary guidelines at all ages.

The observed 0.02–0.03 lower frailty index score from the 'moderately healthy' and 'healthy increased' trajectories in Paper III translates to at least a one-deficit change in the 41-item frailty index (i.e. 1/41 = 0.024). Two studies have identified a 0.03 change in the frailty index score as the minimal change needed to predict 'clinical meaningful changes' in acutely ill, hospitalized patients and community-dwelling older adults, respectively (219, 220). A clinically meaningful change was defined as a noticeable change in patients' health or appearance corresponding to a one-level change in the Clinical Frailty Scale (166, 219), and a change in health-related quality of life after 1 year, measured by the EuroQol-5D instrument (220, 221). This suggests that the observed 0.03 lower frailty index score associated with the 'healthy increased' dietary trajectory in our study may predict long-term improved health-related quality of life. Nevertheless, a 0.03 change in the frailty index does not manifest equally at all levels of frailty and, considering the complexity of the frailty syndrome, the exact impact from any specific change in the frailty index score cannot be established. However, studies have shown that, in community-dwelling older adults, the frailty index increases on average about 3% (i.e. 0.03 frailty index score) annually (222).

5.2.2 Dietary tracking and frailty

One possible advantage of dietary tracking and trajectory analyses, based on repeated measurements of diet over an extended period of time, is the possibility of distinguishing periods when individuals experience significant dietary changes or periods that are more critical than others, in relation to a given outcome (142). For example, the tracking analysis in Paper III could potentially identify whether diet in the first or last period assessed (i.e. between Tromsø4 and Tromsø5 (1994–2001) or between Tromsø5 and Tromsø7 (2001–2015)) was more crucial for frailty development. However, as the dietary trajectories that were significantly associated with frailty in our analysis were either stable or gradually increasing, we saw no such tendencies. In Papers I and II, the lack of identification of any such time period could probably be attributed, to some extent, to the dataset and how the dietary patterns were identified. In Paper I we had only two measurement points of protein

intake and in Paper II we focused on stable patterns, which do not allow for variation in intake, and thus variation between measurement points, over time. Inclusion of several (> 3) repeated measurements of diet would probably offer a more nuanced reflection of the diet over time, however, the dataset did not allow for this. As mentioned, studies examining the association between diet and frailty with long-term follow-up periods are scarce. We argue that our studies, following participants over two decades, contribute valuable and new research to the field.

However, the relevance of the results from the 21-year follow-up analyses may arguably be debated, as it is unknown how motivated and amenable adults in their 40s and 50s are to making dietary changes for their health 20 years later. Research have shown that knowledge alone does not necessarily lead to behaviour changes in individuals, and in particular, when it is not perceived as relevant to them personally or if the impact of change is not sufficiently or immediately noticeable (223). It is possible that Tromsø5 or Tromsø6 would have been more suitable candidates for baseline surveys, conducted 14 and 8 years before follow-up in Tromsø7, respectively, with participants aged ≥ 51 and ≥ 57 years at baseline who might have been more interested in preventing unhealthy ageing than participants aged ≥ 44 years at baseline in Tromsø4. This was the rationale behind choosing Tromsø6 as the baseline survey in Paper II for the analysis of the frequency of fish intake, as we considered intake of fish measured 8 years before follow-up as potentially more clinically relevant than that measured 21 years earlier (in Tromsø4). However, owing to the variations in available data in the surveys, in order to utilize three repeated measurements in the analyses, Tromsø4 had to be included.

5.2.3 Frailty in the Tromsø Study

Using Fried's phenotype, the observed prevalence of frailty and pre-frailty was about 1.0% and 27% in Papers I and II, which is lower than that observed elsewhere in community-dwelling older adults (56, 57). We believe that this is partly the result of selection bias in the study, but also because older Norwegian adults today, in general, are markedly stronger and in better health than previous generations (35). In particular, we suspect that the participants in Tromsø7 were taller and stronger than those in the study by Fried et al. 14 years earlier and, subsequently, that very few were defined as frail with the cut-offs for grip strength and walking speed (Table 2).

Although the frailty index is not primarily meant to be categorized, in Paper III the prevalence of frailty and pre-frailty was drastically higher, at 31% and 62% (using cut-off of 0.1–0.24, data not shown), respectively. This aligns with previous studies that show that the frailty index typically identifies more frail individuals than Fried's definition, although the observed prevalence in our study was higher than observed prevalence of global frailty (14%) and pre-frailty (34%) in older adults, according to a systematic review (56).

We acknowledge that the observed prevalence was surprisingly high, in particular considering the previously low observed frailty prevalence in Tromsø7 in Papers I and II in samples suffering from more or less similar selection bias and inclusion criteria. One possible explanation might be that several of the health deficits in the index were based on multiple questions/measurements, which could have contributed to more participants receiving some frailty score in several variables, than would have been the case if the deficits were based on a single variable. For example, 'anxiety' was defined as a confirmative answer to 'I get sudden feelings of panic', 'I worry all the time' and 'I have felt afraid/anxious during the last week'. We chose to include several subvariables to define the health deficits to minimize the level of missing frailty data. We constructed the frailty index according to an objective framework (46, 51), but how to define the individual health deficits is not specified in the literature. Nevertheless, the frailty index is handled preferably as a continuous, which overcomes the potential risk of misclassification of individuals into the different categories.

Cesari et al. write that, rather than viewing Fried's physical frailty and the frailty index as alternatives, they should be considered as complementary instruments, owing to the conceptual differences that consequently measure different aspects of frailty and identify different groups of individuals (52). This is supported by studies that have shown that, although both instruments identify older people at risk of adverse health outcomes, they identify different subpopulations (224-226). Cesari et al. highlight conceptual differences between the instruments that may contribute to them identifying different aspects of frailty and groups of individuals. For example, Fried's phenotype *does not* include disability and should therefore be applied to non-disabled older adults, whereas the frailty index includes items of functional disability and does not clearly differentiate between frailty and disability (52). Similarly, in our sample in Paper III, participants were classified differently using the frailty index and Fried's frailty, and only 0.6% of the participants were classified as frail and 14% as pre-frail with both definitions (data not shown). As expected, participants were considered frailer using the frailty index compared with the physical phenotype. No

‘physically frail’ participants were robust according to the frailty index, whereas 49% of participants who were robust according to Fried’s frailty were frail according to the frailty index. This is in line with findings from two studies showing that the frailty index is superior in predicting adverse outcomes (225) and mortality risk (226) among pre-frail and robust individuals, respectively. Moreover, two systematic reviews concluded that the frailty index is the favourable outcome instrument as it covers the multidimensionality of frailty better and, with its continuous scoring system, is more sensitive and can discriminate change better after an intervention (227, 228).

6 Conclusions

In the present thesis, longitudinal association between diet, and long-term patterns of diet, and pre-frailty and frailty in Norwegian older adults was investigated, from three different angles. The main conclusions of the three papers are as follows:

- A higher daily protein intake in g/kg bodyweight and maintaining a stable high level of protein intake over 21 years was associated with lower odds of pre-frailty/frailty in older age.

- A frequent intake of lean, fatty and total fish was associated with lower odds of pre-frailty 8 years later. Similarly, a stable high total fish intake over 21 years was associated with lower odds of pre-frailty in older age.

- Eating a diet classified as ‘moderately healthy’ to ‘very healthy’ through adulthood was significantly associated with lower frailty in older age, compared with eating a ‘unhealthy’ diet over time.

In conclusion, our findings consistently show that one’s diet in adulthood may influence health in older age. Specifically, our results indicate that eating a sufficient amount of protein, eating fatty, lean and total fish frequently and eating a diet in line with the NNR2023 may be associated with a lower risk of pre-frailty and frailty in older age. The studies included in this thesis are the first to investigate the association between dietary tracking and trajectories and frailty, showing the importance of maintaining a healthy diet over time. Thus, the results support promotion of a healthy lifestyle and diet, including adherence to dietary guidelines in mid-life, or even earlier, to facilitate healthy ageing and reduce frailty risk in older age.

7 Implications and future perspectives

Because the population as a whole is ageing, our findings are relevant from a public health perspective and, if communicated correctly, comprehensibly and to the right receivers, may contribute to promote healthier ageing in the general population. Our findings suggest that individuals who eat enough protein, fish several times a week and an overall healthy diet, in line with the dietary recommendations, may have good prerequisites for less risk of frailty and healthy ageing in older age. Thus, this is relevant from a cost-effective perspective considering that, if more people remained healthier longer and prolonged the onset of frailty, it would be beneficial financially and in terms of resources.

Our findings also emphasize the value of improving people's diets, if suboptimal, to reduce the risk of frailty in older age. These individuals will need increased knowledge about protein, fish and what constitutes a healthy diet in general, why this is important to them at an individual level and how they realistically and feasibly can make healthy choices in their everyday life, based on their prerequisites.

As is the case for much health-related research, the results of this thesis may be most relevant for those hardest to reach – that is, those who do not themselves seek out knowledge on health and diet from reliable sources or who already prioritize making healthy choices and eating fish, with a healthy and varied diet. Thus, it is particularly important to educate, support and facilitate healthier lifestyles and diets among individuals with low nutrition literacy and those in the lower socioeconomic groups, who typically have poorer health and diet (92).

Promotion of public health by spreading knowledge on how to eat healthily, is the responsibility of dietitians and health care professionals, but, ultimately, of politicians and others who influence the health policy and national and local initiatives to health-promoting measures and activities. Our findings strengthen the argument that it must become easier for individuals to make healthy and long-term choices rather than choices that are unhealthy and – in the long run – harmful to health.

Moreover, we must stop focusing on the 'elderly crisis' ('eldrebølgen' in Norwegian) and the potentially negative aspects of a growing ageing population, but rather work to use this to our advantage. An ageing population is a triumph unparalleled in human history and should be viewed as such. There is an incredible amount of untapped potential in the older population,

but to utilize this and, to a greater extent, include older adults in society requires efforts from politicians, city planners, employers, organizations and the older adults themselves.

This thesis warrants further research to confirm the association between long-term diet and frailty. In particular, there is a need for new studies on dietary trajectories based on multiple measures of diet over time, which may identify time periods and/or life stages crucial for frailty development, or periods when individuals are particularly amenable to dietary intervention and lifestyle change to prevent frailty development.

In addition, future studies should focus on the frailty index and physical pre-frailty, as these are underrepresented in the diet–frailty literature, and also as pre-frail individuals in particular are a more suitable target for preventive measures and interventions than those already physical frail. If possible, future studies should analyse the diet-frailty association for men and women separately, as both diet and frailty differs between the sexes. Moreover, studies should strive to include more heterogeneous study populations, for example, through oversampling of individuals from lower socioeconomic groups or institutions, or by providing these with reimbursement, special assistance or follow-up during the study period.

This also applies to the upcoming Tromsø8 survey. With regard to analyses on diet in the Tromsø Study, a priority in future surveys should, as far as possible, be to collect similar dietary data as in previous surveys, to enable analyses of diet over time based on repeated measurements.

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Paper I

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Original Research

Protein Intake and the Risk of Pre-Frailty and Frailty in Norwegian Older Adults. The Tromsø Study 1994–2016

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Abstract

BACKGROUND: Protein intake is suggested as an important dietary factor in the prevention of frailty, however, the influence of lifelong intake remains unclear.

OBJECTIVES: The present study investigated the relationship between daily protein intake and patterns of protein intake over 21 years and the risk of pre-frailty/frailty.

DESIGN: Prospective cohort study.

SETTING: The population-based Tromsø Study in Tromsø municipality, Norway.

PARTICIPANTS: In total, 1,906 women and 1,820 men aged ≥45 years in 1994 who participated in both Tromsø4 (1994–95) and Tromsø7 (2015–16).

MEASUREMENTS: Frailty status in Tromsø7 was measured according to Fried's phenotype, classifying participants as "robust" (frailty components present: 0), "pre-frail" (1–2) or "frail" (≥3). Daily intake of protein was estimated from self-reported habitual dietary intake using food frequency questionnaires and assessed as grams per kilogram bodyweight (g/kg BW) and per megajoule energy intake (g/MJ). The protein–frailty association was assessed via longitudinal and cross-sectional multivariable logistic regression analyses.

RESULTS: The prevalence of pre-frailty and frailty in this study was 27% and 1.0%, respectively. Longitudinal analysis showed that the odds of pre-frailty/frailty decreased by 57% (odds ratio (OR) = 0.43, 95% confidence interval (CI) = 0.31;0.58, p<0.001) with the increase in intake of one additional gram of dietary protein per kg BW. The results obtained from cross-sectional analysis were similar. Tracking analysis showed that, compared to a stable high intake of protein in g/kg BW over time, other patterns of protein intake increased the risk of pre-frailty/frailty. No associations were found between intake of protein in g/MJ and pre-frailty/frailty.

CONCLUSIONS: Intake of protein in g/kg BW both in mid-life and later in life was inversely associated with pre-frailty/frailty in older adults. This emphasizes the importance of an adequate protein intake to facilitate healthy ageing in Norwegian older adults.

Key words: Frailty, pre-frailty, protein, nutrition, older adults.

Introduction

A growing ageing population with subsequent age-associated deteriorating health represents one of the most prominent health challenges of the twenty-first century (1). As the proportion of older adults ≥65 years increases (1), the prevalence of the geriatric syndrome frailty is likely to increase accordingly. Frail individuals experience increased vulnerability to stressors and are at higher risk of negative health outcomes including falls, disability, institutionalization and mortality (2, 3).

Despite the lack of consensus in the definition of frailty, a diversity of scales and indices exists for its operationalization (4). The most widely used definition (4) of physical frailty is the presence of three or more of the five frailty phenotype components proposed by Fried and colleagues in 2001 (3): unintentional weight loss, exhaustion, weakness, slow walking speed and a low physical activity level. The presence of one or two of these criteria indicates pre-frailty, an intermediate stage in which individuals are at high risk of progressing to frailty (5). Owing to the fluctuating nature of the frailty syndrome, these states are also transitional, and therefore, potentially reversible (6).

Poor nutrition is identified as an important modifiable risk factor for frailty, and all components of the frailty phenotype may be influenced directly by this factor (7). Maintenance of a healthy diet is key for preservation of independence during ageing, and in particular a high protein intake has been associated with better physical performance and a lower prevalence of frailty (7-10). Adequate intake of protein contributes to preservation of the muscle protein synthesis and slows down age-associated muscle degeneration and the development of sarcopenia, which facilitates maintenance of muscle mass, physical activity and reduces weight loss (10, 11).

Although several longitudinal (11-15) and cross-sectional (16-18) studies have shown a protective effect of protein consumption on the risk of frailty, other studies have observed no relationship at all (19, 20). The use of study-specific definitions of frailty, and different cut-offs and units to assess protein intake, hampers comparisons among studies (10). Further, most studies on protein intake and risk of frailty have a cross-sectional study design and there are few longitudinal studies with long periods of follow-up (10). Therefore, longitudinal studies are needed to elucidate further the potential role of lifelong protein intake on the risk of frailty.

The aims of the present study were to assess the impact of both previous and current daily intake of protein, as well as tracking patterns of protein intake over 21 years, on the risk of pre-frailty/frailty in Norwegian older adults.

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Methods

The Tromsø Study

Data were obtained from the longitudinal population-based Tromsø Study conducted in the municipality of Tromsø, Norway (21). The Tromsø Study consists of seven surveys (Tromsø1–7) carried out between 1974 and 2016, in which full birth cohorts and random samples of the population were invited to participate. In total, 45,473 men and women have participated in one or more of the surveys (participation rate 65%–79%). Data were collected via interviews, questionnaires, physical examinations and biological sampling (21). The present study includes data from Tromsø4 (1994–95) and Tromsø7 (2015–16), the only two study waves in which nutritional intake was estimated.

Study sample

In Tromsø4 (1994–95), all inhabitants aged ≥25 years (N=37,558) were invited, and 27,158 (72%) participated (22). Invitations were sent by mail accompanied by a short questionnaire, which the participants completed before attendance. At the examination site, participants were given a more comprehensive questionnaire, which included questions about diet, to be completed during the visit or afterwards at home and returned by mail, and they underwent physical examinations including measurement of height in metres (m) and BW in kg in light clothing without shoes (22).

In Tromsø7 (2015–16), all inhabitants ≥40 years (N=32,591) were invited, and 21,083 (65%) participated (23). On attendance, a sub-sample (n=9,324), were invited to undergo extended examinations (a second visit) approximately two weeks later, in which 8,346 (90%) people attended. This sub-sample consisted of randomly selected participants plus a small extra sample of participants in previous Tromsø studies. For the main examination, participants received invitations by mail with a short printed questionnaire and log-in details to complete this and additional questionnaires online (23). The questionnaires were to be completed before attendance, but technical support was available at the examination site. Participants were subjected to measurements of height and BW, as in Tromsø4, and they received a comprehensive paper-based food frequency questionnaire (FFQ) to be completed during the visit or at home and returned by mail. Participants who attended the second visit underwent comprehensive physical examinations, including measurements of grip strength and walking speed (23).

The present study includes participants from Tromsø4 aged 45–69 years who had participated in Tromsø7 and had data on a minimum of three out of five frailty criteria in Tromsø7. Participants without valid estimated protein intake either in Tromsø4 or in Tromsø7 were excluded, as were participants with energy intakes outside the study-specific cut-offs. In total, 3,726 participants constituted the main analytical sample. For the statistical tests, the sample size was further reduced depending on whether the analyses included estimated protein intake at baseline (n=3,089), follow-up (n=2,507), or at both time points (n=1,908) (Figure 1).

Dietary assessment

Calculations of baseline daily nutrient intake in Tromsø4 were based on self-reported intake of 34 food items from the two study questionnaires provided. Nutrient estimations were performed for those who had answered at least 31 of the 34 questions. Participants with energy intakes outside the <1 (<3,822 kJ/day (914 kilocalories (kcal)/day)) and >99 percentiles (>13,660 kJ/day (3265 kcal/day)) identified from the whole Tromsø4 population were excluded, in accordance with Jacobsen and Nilsen (24). Portion sizes were estimated for each sex on the basis of data from previous dietary surveys in Northern Norway (25, 26). The Norwegian food composition table from 1995 (27) provided the basis for calculations of nutrient intake, supplemented with data from the corresponding Swedish food composition table in the case of missing food composition values (28). A more detailed description of the food and nutrient estimates for Tromsø4 is available in Jacobsen and Nilsen (24).

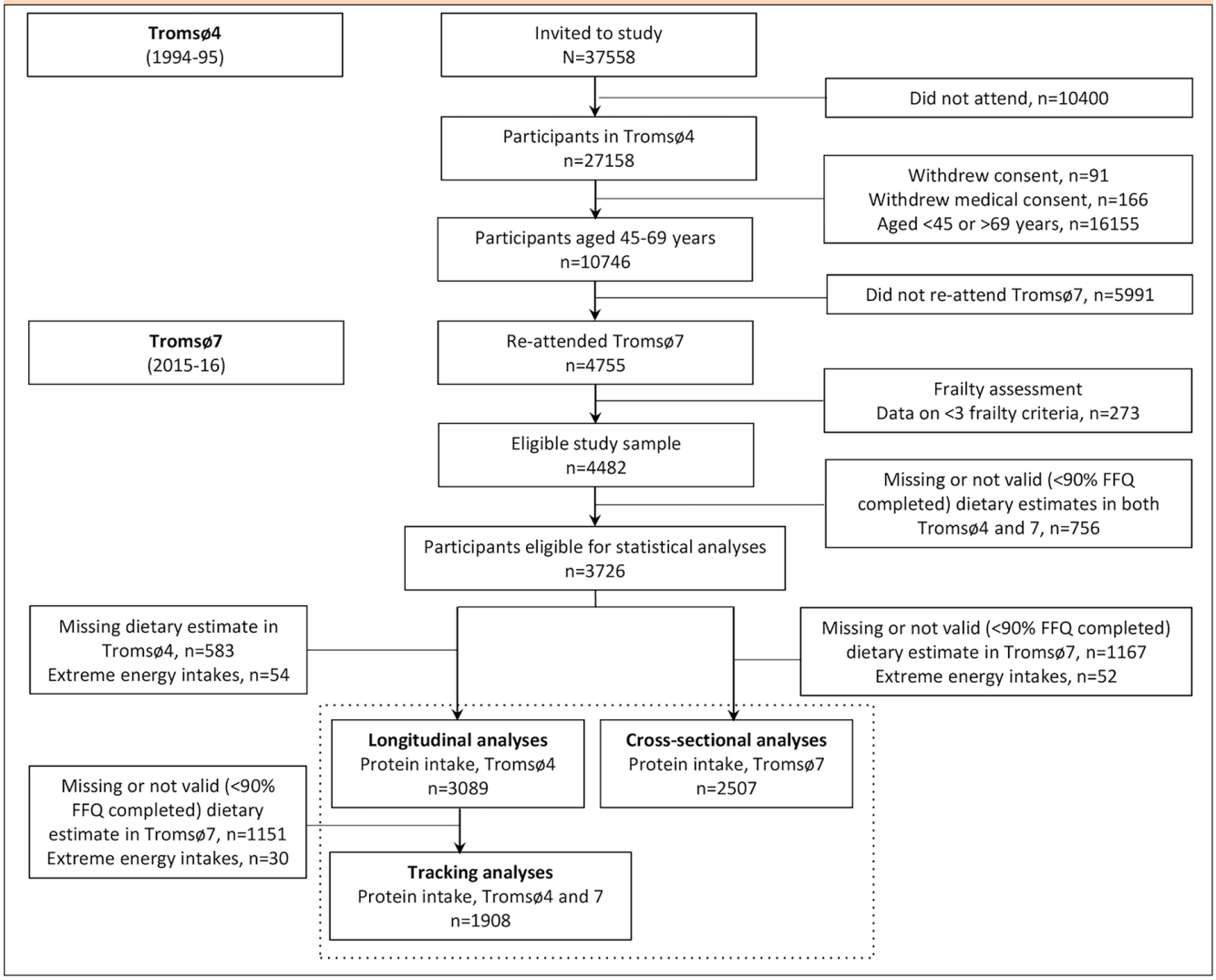
In Tromsø7, the follow-up nutritional estimates were based on an FFQ developed at the University of Oslo (UiO), designed to collect information on the total diet, including questions on frequency and amount of intake of 261 dietary items (29). Participants who completed less than 90% of the FFQ were excluded, as were participants with extreme energy intakes (<3,948 kJ/day and >21,267 kJ/day (944 kcal/day and 5083 kcal/day)), in accordance with Lundblad et al. (29). Daily intakes of energy and protein were calculated using the food and nutrient calculation system KBS, with database version AE14 at the UiO (KBS, version 7.3.). The food database KBS AE14 is based on the 2014–15 edition of the Norwegian food composition table (http://www.norwegianfoodcomp.no) and supplementary data calculated from recipes and additional databases (30).

Average daily protein intake was expressed in grams (g), grams per megajoule total energy intake (g/MJ), and grams per kilogram bodyweight (g/kg BW). Intake of protein when expressed as g/MJ reflects the proportion of protein in a person's diet while intake in g/kg BW reflects protein intake relative to BW.

Dietary tracking

For tracking analyses, the participants were allocated to study-specific tertiles of protein intake at baseline and follow-up. Subsequently, the proportion of pre-frail/frail and robust participants with a stable or changed level of protein intake from Tromsø4 to Tromsø7 was identified by cross-tabulation. Stability was presented as the proportion of participants who remained in the same tertile of protein intake between time points, and change was presented as the proportion of participants who decreased or increased their associated tertile of protein intake over time. Tracking coefficients were calculated for each of the two protein variables for pre-frail/

Figure 1. Flow chart of included participants



Dashed line marks sub-samples of participants included in statistical analyses

frail and robust participants separately using Cohen's weighted kappa (ϰw) (31). This is a measure of the level of agreement between tertile memberships at different time points, with membership of the same tertile considered to be perfect agreement and different weighting to movements between adjacent-versus-extreme tertiles (31). Cut-offs proposed by Landis and Koch (32) were used for the interpretation of kappa values. For the logistic regression analyses, a variable of four tracking groups was created: stable low intake (low and medium tertiles), stable high intake (highest tertile), and decreased and increased level of protein intake between Tromsø4 and Tromsø7. The stable high intake was set as the reference category.

Frailty measurement

A modified version of the physical frailty phenotype described by Fried et al. (3) was used to assess frailty in Tromsø7 (Supplementary Table 1). Baseline frailty status was not assessed in Tromsø4 owing to insufficient data.

A low physical activity level was defined as the lowest category, "Mainly reading, watching TV/screen or other sedentary activity", in the four-level Saltin-Grimby Physical Activity Level Scale (33). Weight loss was defined by the Malnutrition Universal Screening Tool (34) as self-reported involuntary weight loss during the previous 6 months. Exhaustion was defined by a single item from the Hopkins Symptoms Checklist 10 (35): "Have you felt that everything is a struggle during the last week?", as the two highest categories, "Pretty much" or "Very much". Low walking speed was defined in accordance with cut-offs for frailty as proposed by Fried et al. (3) using the short physical performance battery test (36). Participants were asked to walk 4 m at their average speed twice, of which the fastest test was recalculated as seconds per 4.752 m (15 feet), and adjusted for sex and height to match the definition of Fried et al. (3). Grip strength (kg) was measured using a Jamar (PLUS+) electric dynamometer. The strongest of three measurements on each hand was recorded as the maximal

grip score, as according to the Southampton protocol (37). Low grip strength was defined in accordance with cut-offs for frailty as proposed by Fried et al. (3). For men, low grip strength was defined accordingly for the body mass index (BMI) quartiles; ≤24, 24.1–26, 26.1–28 and >28 when accompanied by grip strengths (kg) ≤29, ≤30, ≤30, ≤32, respectively. For women, the corresponding cut-offs were ≤23, 23.1–26, 26.1–29, >29 and ≤17, ≤17.3, ≤18, ≤21, respectively. BMI was calculated as measured BW divided by the square of a person's height (kg/m^2).

Participants who fitted none of the above criteria were considered robust, those scoring 1–2 were considered pre-frail, while those with a score ≥3 were considered frail. Given the low number of participants with frailty score ≥3 (n=36), the outcome assessed in this study was pre-frail and frail combined (frailty score ≥1).

Covariates

Baseline (Tromsø4) covariates were selected for descriptive purposes and as potentially confounding factors based on existing literature. Sociodemographic characteristics and lifestyle factors were self-reported by participants in the questionnaires provided.

Smoking status was divided into three groups: never smoked, current daily smoker, and previous daily smoker. Cohabitation was defined based on a combination of the participant's marital and living status. Participants who were married or living with their spouse/partner, were classified as cohabitants. Level of education was grouped into four categories: 1) primary/(modern) secondary school (7–10 years) , 2) technical/vocational/middle school, 1–2 years senior high school, high school diploma, 3) college/university <4 years and 4) college/university ≥4 years. The question "Do you feel that you have enough good friends?", ("yes"/"no") was included as a measure of the level of social capital and support. Participants were classified as physically active if they reported performing hard physical activity weekly, with sweating or breathlessness, or ≥3 hours weekly of light activity without sweating or breathlessness. Comorbidity was defined as the self-reported presence of two or more of the following diseases: coronary heart disease (angina pectoris and/or heart attack), stroke, pulmonary disease (asthma and/or chronic bronchitis), peptic ulcer (gastric and/or duodenal ulcer), cancer and diabetes, based on the Charlson Comorbidity Index without weigthing of diseases (38). High alcohol consumption was defined as estimated intake above the upper recommended daily limits set out by the Norwegian Directorate of Health at ≥10 g for women and ≥20 g for men (39). The same characteristics were obtained for participants at follow-up (Tromsø7) for sensitivity analyses and descriptive purposes, with the exception of peptic ulcer owing to a lack of information.

Statistical analysis

Differences between pre-frail/frail and robust groups were tested using the Student's t-test for continuous variables and the chi-square or Fisher's exact test for categorical variables. Continuous variables are presented as means and standard deviations or 95% confidence intervals (CIs). Categorical variables are presented as counts and proportions.

The association between protein intake and pre-frailty/frailty was examined via multivariable logistic regression analysis in three ways: 1) longitudinal analyses on baseline (Tromsø4) protein intake and 21-year follow-up (Tromsø7) frailty status, 2) cross-sectional analyses on Tromsø7 protein intake and frailty status, and 3) longitudinal analyses on tracking patterns of protein intake between Tromsø4 and Tromsø7, and Tromsø7 frailty status. All effect estimates are presented as odds ratios (OR) with 95% CI.

Primary analyses were solely adjusted for age (Model 1) and subsequently further for baseline (Model 2) and follow-up covariates (Model 4), respectively. The main analytic model, Model 2, was adjusted for age, sex and baseline smoking status, education level, and BMI. Model 4 was adjusted for age, sex and follow-up smoking status, comorbidity and BMI. Multivariable analyses on protein expressed as g/kg BW were not adjusted for BMI. However, to assess the potential influence of energy intake, Models 3 and 5 were additionally adjusted for baseline and follow-up daily energy intake, respectively.

Several supplementary analyses were performed. To assess potential influence of follow-up protein intake, supplementary longitudinal logistic regression analyses were additionally adjusted for Tromsø7 protein intake (Models 6, 7). To account for possible misclassification of participants of robust participants with missing frailty data (n=910), frailty was imputed in individual frailty items in these participants. Imputation was done manually in 25% (n=228), 50% (n=455), 75% (n=683) and 100% (n=910) of cases. Subsequently, Model 2 was run in these four hypothetical study populations. To elucidate further the protein–frailty association, Models 1 and 2 were run on protein intake and frailty score ≥2, and low grip strength, respectively. Analyses on frailty score ≥2 excluded participants with frailty score 1 and were run to further account for possible misclassification given that these constituted the vast majority of the pre-frail/frail group. Low grip strength was chosen among the five frailty criteria as a proxy for muscle function.

The multivariable model was built using purposeful selection method with protein intake (g/MJ) as the key exposure variable (40, 41). Following univariate analyses of the covariates previously described, variables with p-values <0.20 or with known clinical relevance (sex) were selected for further inclusion.

Specific diseases were not included in the univariate analysis, only the comorbidity variable as a proxy for disease status. After identification of nonlinear tendencies of the continuous variables age and BMI, these were additionally added to the model in their quadratic forms. No statistically significant interactions were found between biologically plausible variables. All statistical analyses were performed in STATA 16.5. A p-value of <0.05 was considered statistically significant.

Table 1. Baseline (Tromsø4) characteristics of study participants by Tromsø7 frailty status (n=3726)

Baseline characteristics	All (n=3726)			Women (n=1906)			Men (n=1820)		
	Robust (n=2681)	Pre-frail/frail (n=1045)	P*	Robust (n=1343)	Pre-frail/frail (n=563)	P*	Robust (n=1338)	Pre-frail/frail (n=482)	P*
Attendees, %	72.0	28.0		70.5	29.5		73.5	26.5	
Age (years), mean (sd)	50.9 (4.9)	52.3 (5.6)	<0.001	50.6 (4.9)	52.2 (5.6)	<0.001	51.1 (4.9)	52.4 (5.6)	<0.001
Weight (kg), mean (sd)	73.8 (12.6)	75.4 (13.9)	<0.001	66.6 (10)	68.9 (11.6)	<0.001	81.1 (10.4)	82.9 (12.6)	0.002
Height (cm), mean (sd)	171 (8.9)	169 (9.5)	<0.001	164 (5.9)	163 (6.4)	<0.001	177 (6.3)	177 (6.9)	0.08
BMI (kg/m^2), mean (sd)	25.3 (3.3)	26.3 (3.8)	<0.001	24.7 (3.6)	26.0 (4.1)	<0.001	25.8 (2.8)	26.6 (3.4)	<0.001
Daily smoking, n (%)	2677	1045		1341	563		1336	482	
Currently, n (%)	744 (27.8)	381 (36.5)	<0.001	369 (27.5)	204 (36.2)	0.001	375 (28.1)	177 (36.7)	0.001
Previously, n (%)	963 (36.0)	347 (33.2)		404 (30.1)	158 (28.1)		559 (41.8)	189 (39.2)	
Never, n (%)	970 (36.2)	317 (30.3)		568 (42.4)	201 (35.7)		402 (30.1)	116 (24.1)	
Married or cohabitation, n (%)	2292 (88.5)	864 (86.6)	0.12	1101 (85.5)	449 (84.2)	0.50	1191 (91.4)	415 (89.3)	0.17
Education†, n (%)	2675	1043		1340	561		1335	481	
Primary/partly secondary, n (%)	822 (30.7)	400 (38.4)		461 (34.4)	264 (47.0)		361 (27.0)	136 (28.3)	
Upper secondary, n (%)	937 (34.7)	372 (35.7)	<0.001	475 (35.5)	194 (34.5)	<0.001	452 (33.9)	178 (37.0)	0.18
Short tertiary, n (%)	466 (17.4)	146 (14.0)		186 (13.9)	46 (8.2)		280 (21.0)	100 (20.8)	
Long tertiary, n (%)	460 (17.2)	125 (12.0)		218 (16.3)	58 (10.3)		241 (18.1)	67 (13.9)	
Social support‡, n (%)	2071 (82.4)	793 (80.3)	0.16	1074 (85.4)	439 (82.4)	0.10	997 (79.3)	354 (78.0)	0.55
Good self-rated health, n (%)	2053 (76.7)	660 (63.2)	<0.001	968 (72.2)	318 (56.6)	<0.001	1085 (81.2)	342 (71.0)	<0.001
Physically active, n (%)	1881 (70.2)	603 (57.7)	<0.001	869 (64.8)	310 (55.1)	<0.001	1012 (75.6)	293 (60.9)	<0.001
High alcohol consumption§, n (%)	44 (2.0)	23 (2.6)	0.26	25 (2.2)	10 (2.1)	0.92	19 (1.7)	13 (3.1)	0.08
Comorbidity, n (%)	46 (1.7)	26 (2.5)	0.12	19 (1.4)	13 (2.3)	0.17	27 (2.0)	13 (2.7)	0.38
Coronary heart disease‖, n (%)	62 (2.3)	44 (4.2)	0.002	12 (0.9)	13 (2.3)	0.01	50 (3.7)	31 (6.5)	0.01
Pulmonary disease{, n (%)	213 (8.0)	98 (9.4)	0.16	115 (8.6)	59 (10.5)	0.19	98 (7.3)	39 (8.1)	0.58
Peptic ulcer#, n (%)	169 (6.8)	88 (9.0)	0.03	70 (5.7)	38 (7.2)	0.20	99 (7.9)	50 (11.1)	0.04
Cancer, n (%)	65 (2.6)	31 (3.1)	0.38	53 (4.3)	19 (3.6)	0.52	12 (0.9)	12 (2.6)	0.01
Stroke, n (%)	13 (0.5)	8 (0.8)	0.30	6 (0.5)	3 (0.5)	**	7 (0.5)	5 (1.0)	0.23
Diabetes, n (%)	11 (0.4)	6 (0.6)	0.50	5 (0.4)	3 (0.5)	**	6 (0.5)	3 (0.6)	**

BMI: body mass index, sd: standard deviation, MJ: megajoule, BW: bodyweight. N deviates slightly owing to a lack of data on specific variables. *P-value from Student's t-test for continuous variables and chi-square test for categorical variables between pre-frail/frail and robust women and men. †Primary/secondary school 7–10 years, modern secondary school; technical/vocational/middle school, 1–2 years senior high school or high school diploma (3–4 years); college/university <4 years; college/university ≥4 years. ‡Self-reported satisfactory number of good friends. §Daily alcohol intake ≥10 g (women) or ≥20 g (men). ‖Angina pectoris and/or myocardial infarction. {Asthma and/or chronic bronchitis. #Gastric and/or duodenal ulcer. **No chi-square test performed owing to low n (<5) in cell.

Results

Characteristics

The mean age at follow-up was 73 years (Supplementary Table 2). Thirty-six participants (1.0%) were classified as frail and 1,009 (27%) as pre-frail, totalling 1,045 (28%) pre-frail/frail. The prevalence of frailty and pre-frailty increased with age (p<0.001) (Supplementary Table 3).

At baseline, pre-frail/frail participants were slightly older and had higher BW and BMI compared with robust participants, both when all participants were combined, and when stratified by sex (Table 1). A higher proportion of pre-frail/frail than robust participants were daily smokers (37% vs 28%) at baseline, while more robust participants considered their own health as good (77% vs 63%) and were physically active (70% vs 58%). At baseline, pre-frail/frail women were more likely to have the lowest level of education (47% vs 38%). Pre-frail/frail and robust participants did not differ at baseline in terms of cohabitation, self-perceived social support, alcohol consumption or comorbidity, either when men and women were combined or considered separately (Table 1).

Also at follow-up, pre-frail/frail participants had higher BW and BMI than robust participants (Supplementary Table 2). Compared with robust participants, more pre-frail/frail participants were daily smokers (15% vs 8.0%) and suffered from comorbidity (21% vs 13%), while fewer were satisfied with their own health (45% vs 71%). Pre-frail/frail women were more likely to have completed the lowest level of education (57% vs 43%) and less likely to have high alcohol consumption (17% vs 29%) compared with robust women (Supplementary Table 2).

Tromsø4 participants who did not attend Tromsø7 (n=5,991) were older, had higher BMI, were less physically active (57% vs 65%), had higher prevalence of comorbidity (7.0% vs 2.2%) and slightly higher intake of protein in g/MJ in Tromsø4 compared with those who did (n=4,755) (Supplementary Table 3).

Table 2. Daily nutrient intake in Tromsø4 and Tromsø7 by follow-up (Tromsø7) frailty status (n=3726)

	All (n=3726)			Women (n=1906)			Men (n=1820)		
	Robust	Pre-frail/frail		Robust	Pre-frail/frail		Robust	Pre-frail/frail	
	Mean (95% CI)	Mean (95% CI)	P*	Mean (95% CI)	Mean (95% CI)	P*	Mean (95% CI)	Mean (95% CI)	P*
Tromsø4, n=3089	2220	869		1113	457		1107	412	
Energy, MJ	7.96 (7.88;8.05)	7.70 (7.57;7.84)	0.002	6.82 (6.73;6.91)	6.57 (6.44;6.70)	0.004	9.11 (9.00;9.22)	8.96 (8.78;9.13)	0.15
Protein, g	78.3 (77.5;79.1)	76.6 (75.2;77.9)	0.03	67.6 (66.7;68.4)	65.2 (64.0;66.4)	0.003	89.1 (88.1;90.2)	89.1 (87.4;90.9)	0.99
Protein, g/MJ	9.95 (9.90;10.0)	10.0 (9.95;10.1)	0.09	10.0 (9.95;10.1)	10.0 (9.91;10.2)	0.96	9.87 (9.79;9.94)	10.0 (9.91;10.2)	0.02
E%	16.6 (16.6;16.7)	16.8 (16.6;16.9)	0.09	16.8 (16.6;16.9)	16.8 (16.6;17.0)	0.96	16.5 (16.4;16.6)	16.8 (16.6;17.0)	0.02
Protein, g/kg BW	1.08 (1.07;1.09)	1.03 (1.01;1.05)	<0.001	1.04 (1.02;1.05)	0.97 (0.95;1.00)	<0.001	1.12 (1.10;1.14)	1.10 (1.07;1.12)	0.11
Tromsø7, n=2507	1834	673		893	359		941	314	
Energy, MJ	9.20 (9.07;9.33)	8.70 (8.50;8.91)	<0.001	8.50 (8.33;8.67)	8.01 (7.78;8.32)	0.005	9.86 (9.68;10.0)	9.45 (9.15;9.75)	0.03
Protein, g	95.6 (94.2;97.0)	90.3 (88.0;92.5)	<0.001	89.7 (87.8;91.6)	83.7 (89.7;86.8)	0.001	101 (99.3;103)	97.7 (94.5;101)	0.08
Protein, g/MJ	10.5 (10.4;10.5)	10.4 (10.3;10.5)	0.66	10.6 (10.5;10.7)	10.4 (10.3;10.6)	0.09	10.3 (10.2;10.4)	10.4 (10.3;10.6)	0.35
E%	17.5 (17.4;17.6)	17.5 (17.2;17.6)	0.66	17.7 (17.5;17.9)	17.4 (17.2;17.7)	0.09	17.3 (17.1;17.4)	17.4 (17.1;17.7)	0.35
Protein, g/kg BW	1.27 (1.25;1.29)	1.17 (1.14;1.20)	<0.001	1.31 (1.28;1.34)	1.17 (1.12;1.22)	<0.001	1.22 (1.20;1.25)	1.17 (1.23;1.21)	0.04
Participants in tracking analysis (n=1908)									
Tromsø4	1401	507		680	259		721	248	
Energy, MJ	8.01 (7.90;8.11)	7.78 (7.61;7.95)	0.03	6.85 (6.73;6.97)	6.68 (6.51;6.86)	0.13	9.09 (8.97;9.22)	8.92 (8.71;9.14)	0.19
Protein, g	78.5 (77.5;79.5)	77.3 (75.6;78.9)	0.21	67.6 (66.6;68.7)	66.3 (64.6;68.0)	0.19	88.8 (87.5;90.0)	88.7 (86.6;90.9)	0.99
Protein, g/MJ	9.91 (9.85;9.98)	10.0 (9.91;10.2)	0.08	9.99 (9.89;10.1)	10.0 (9.87;10.2)	0.70	9.84 (9.75;9.93)	10.0 (9.86;10.2)	0.04
E%	16.6 (16.5;16.7)	16.8 (16.6;17.0)	0.08	16.7 (16.6;16.9)	16.8 (16.5;17.1)	0.70	16.5 (16.3;16.6)	16.8 (16.5;17.1)	0.04
Protein, g/kg BW	1.09 (1.07;1.10)	1.03 (1.08;1.05)	<0.001	1.05 (1.02;1.07)	0.98 (0.94;1.01)	<0.001	1.12 (1.10;1.14)	1.09 (1.06;1.12)	0.14
Tromsø7	1401	507		680	259		721	248	
Energy, MJ	9.23 (9.09;9.38)	8.77 (8.53;9.01)	0.001	8.61 (8.42;8.80)	8.05 (7.76;8.36)	0.003	9.82 (9.62;10.0)	9.52 (9.18;9.86)	0.14
Protein, g	95.5 (93.9;97.0)	90.9 (88.3;93.5)	0.003	90.5 (88.4;92.7)	83.8 (80.3;87.3)	0.002	100 (98.0;102)	98.3 (94.7;102)	0.41
Protein, g/MJ	10.4 (10.3;10.5)	10.4 (10.3;10.6)	0.65	10.5 (10.4;10.7)	10.4 (10.3;10.6)	0.32	10.3 (10.2;10.4)	10.4 (10.2;10.6)	0.12
E%	17.4 (17.3;17.5)	17.4 (17.2;17.7)	0.65	17.6 (17.5;17.8)	17.5 (17.1;17.8)	0.32	17.2 (17.0;17.3)	17.4 (17.1;17.8)	0.12
Protein, g/kg BW	1.27 (1.25;1.29)	1.16 (1.13;1.20)	<0.001	1.33 (1.30;1.36)	1.15 (1.10;1.21)	<0.001	1.21 (1.19;1.24)	1.17 (1.12;1.22)	0.12

CI: confidence interval, MJ: megajoule, E%: proportion of total energy from protein, BW: bodyweight. N deviates slightly owing to a lack of data on specific variables. Data shown as means and 95% confidence intervals. *P-value from Student's t-test between daily protein intake and frailty status.

Protein intake

Mean daily protein intake for all participants was 78 g at baseline (Tromsø4) and 93 g at follow-up (Tromsø7) (Table 2). Also, in Tromsø4, mean daily intake was 1.1 g/kg BW and 17 E%, whereas in Tromsø7 the corresponding values were 1.2 g/kg BW and 18 E%, respectively. Both pre-frail/frail and robust participants had higher total and relative daily intake of protein at follow-up (Tromsø7) than at baseline (Tromsø4).

Overall, robust participants had a higher daily intake of protein in g and g/kg BW compared to pre-frail/frail participants at baseline and follow-up (Table 2). In women, robust participants had a higher daily intake of total protein and protein expressed as g/kg BW compared with pre-frail/frail women at baseline (68 g vs 65 g, p=0.003; 1.04 vs 0.97 g/kg BW, p<0.001) and follow-up (90 g vs 84 g, p=0.001; 1.31 vs 1.17 g/kg BW, p<0.001). In men, a marginally higher baseline intake of protein expressed as g/MJ was observed in pre-frail/frail men, compared with robust men (100 vs 99 g/MJ, p=0.02). At follow-up, robust men had slightly higher intake of protein expressed as g/kg BW compared with pre-frail/frail men (1.22 vs 1.17 g/kg BW, p=0.04) (Table 2).

The sub-sample of participants included in the tracking analyses (Figure 1) resembled the main samples with higher observed intakes at follow-up than at baseline (Table 2). Moreover, differences in protein intake between robust and pre-frail/frail groups in the tracking sub-sample were largely similar as described above, except for intake of total protein, which was less likely to differ significantly between groups.

For the tracking of intake of protein expressed as g/kg BW, a trend was observed in which more pre-frail/frail participants had a stable low than high level of intake (53% vs 39%), and a decreased rather than increased (30% vs 27%) tertile of intake (Table 3). In robust participants, a slightly higher proportion had a stable high than low level of intake of protein in g/kg BW (51% vs 49%) between time points. No clear trend was observed for patterns of intake of protein when expressed as g/MJ. Tracking coefficients measured by Cohen's weighted kappa (0.18–0.25) indicated overall slight to fair tracking of protein intake between time points (Table 3).

Protein intake and risk of pre-frailty/frailty

Longitudinal analyses of protein intake in Tromsø4, expressed as g/kg BW, and pre-frailty/frailty in Tromsø7 showed lower odds of pre-frailty/frailty with increased protein

Table 3. Tracking values and proportion of stability of protein intake in pre-frail/frail and robust participants between Tromsø4 and Tromsø7 (n=1908)

Protein intake	Tromsø4			Tromsø7			
	n (%)	Decrease II tertiles, n (%)*	Decrease I tertile, n (%)*	Stability, n (%)†	Increase I tertile, n (%)*	Increase II tertiles, n (%)*	Cohen's Kw‡
Protein intake, g/MJ							
Robust participants	1401						
Low (<9.3)	470 (33.6)	nc	nc	223 (47.4)	160 (34.0)	87 (18.5)	
Medium (9.3–10.4)	482 (34.4)	nc	146 (30.3)	174 (36.1)	162 (36.1)	nc	**0.20**
High (>10.4)	449 (32.0)	99 (22.0)	147 (32.7)	203 (45.2)	nc	nc	
Pre-frail/frail participants	507						
Low (<9.3)	166 (32.7)	nc	nc	76 (45.8)	51 (30.7)	39 (23.5)	
Medium (9.3–10.4)	154 (30.4)	nc	51 (33.1)	46 (29.9)	57 (37.0)	nc	**0.18**
High (>10.4)	187 (36.9)	41 (21.9)	58 (31.0)	88 (47.1)	nc	nc	
Protein intake, g/kg BW							
Robust participants	1401						
Low (<0.9)	433 (30.9)	nc	nc	214 (49.4)	127 (29.3)	92 (21.2)	
Medium (0.9–1.2)	478 (34.1)	nc	141 (29.5)	177 (37.0)	160 (33.5)	nc	**0.25**
High (>1.2)	490 (35.0)	73 (14.9)	165 (33.7)	252 (51.4)	nc	nc	
Pre-frail/frail participants	507						
Low (<0.9)	203 (40.0)	nc	nc	107 (52.7)	60 (29.6)	36 (17.7)	
Medium (0.9–1.2)	158 (31.2)	nc	65 (41.1)	54 (34.2)	39 (24.7)	nc	**0.19**
High (>1.2)	146 (28.8)	36 (24.7)	53 (36.3)	57 (39.0)	nc	nc	

MJ: megajoule, BW: bodyweight. nc: no possible change (decrease/increase) in level of intake. *Proportion of participants who changed tertile of protein intake from Tromsø4 to Tromsø7. †Proportion of participants who remained in the same tertile of protein intake from Tromsø4 to Tromsø7. ‡Tracking coefficient of weighted Cohen's kappa.

intake both in primary (Model 1) and fully adjusted analyses (Model 2) (OR=0.43, 95%CI=0.31;0.58, p<0.001) (Table 4). Similarly, cross-sectional analyses of protein intake in Tromsø7, expressed as g/kg BW, showed an inverse association with odds of pre-frailty/frailty after adjusting for baseline covariates (Model 2) (OR=0.57, 95%CI=0.46;0.72, p<0.001). All findings remained significant following adjustment for follow-up covariates (Model 4) and/or energy intake (Models 3, 5) (Table 4).

Results from tracking analyses of protein intake, expressed as g/kg BW, showed that participants with a stable low intake or who changed their tertile of protein intake between time points had higher odds of pre-frailty/frailty than those with a stable high level of intake. Specifically, a stable low protein intake (OR=1.96, 95%CI=1.38;2.78, p<0.001), a decreased (OR=1.73, 95%CI=1.22;2.46, p=0.002) or an increased tertile of protein intake over time (OR=1.70, 95%CI=1.20;2.44, p=0.004) increased the risk of pre-frailty/frailty in Tromsø7 (Model 2, Table 4). Following additional adjustment for energy intakes, the patterns increased and decreased level of protein intake (in g/kg BW) were not significantly (Model 3) and borderline significantly (Model 5) associated with pre-frailty/frailty in Tromsø7 (Table 4).

For intake of protein in g/MJ, age-adjusted tracking analysis (Model 1) showed that participants with a stable low intake over time had lower odds of pre-frailty/frailty in Tromsø7 (OR=0.67, 95%CI=0.48;0.92, p=0.02) than participants with a stable high intake, although this was no longer significant after further adjustments (Table 4). No other associations were found between intake of protein in g/MJ and pre-frailty/frailty in Tromsø7.

Supplementary analyses with additional adjustment for protein intake in Tromsø7 supported the findings of an inverse association between intake of protein in g/kg BW and risk of pre-frailty/frailty (Supplementary Table 5). Similarly, sensitivity analyses with imputed frailty data showed lower odds of pre-frailty/frailty with increased daily intake of protein in g/kg BW, at all levels of imputation. Also, with imputations, the only patterns of protein intake associated with increased risk of pre-frailty/frailty were a stable low, and a decreased level of intake (Supplementary Table 6). Results were similar for sensitivity analyses on daily intake of protein in g/kg BW and frailty score ≥2. A stable low level of intake was associated with increased risk of frailty score ≥2 (Supplementary Table 7). For low grip strength, cross-sectional analyses showed an inverse association with daily intake of protein in g/kg BW. Tracking analyses showed higher odds of low grip strength in Tromsø7 in participants with decreased level of protein intake over time (Supplementary Table 8).

Discussion

Daily intake of protein expressed as g/kg BW in adulthood and older age was inversely associated with risk of pre-frailty/frailty in older age. Tracking analysis showed that, compared to a stable high intake of protein in g/kg BW over time, different patterns of protein intake increased the risk of pre-frailty/frailty.

Table 4. Odds ratios (OR) and 95% confidence intervals (CI) for daily intakes of protein in Tromsø4, and Tromsø7, tracking patterns of protein intake from Tromsø4 to Tromsø7, and pre-frailty/frailty in Tromsø7 (n=3726)

Dietary exposure	Model 1			Model 2*			Model 3*			Model 4*			Model 5*		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Daily intake Tromsø4, n=3089†															
Protein, g/MJ	1.04	0.98;1.11	0.17	1.00	0.93;1.06	0.88				1.00	0.94;1.07	0.97			
Protein, g/kg BW	0.47	0.34;0.63	<0.001	0.43	0.31;0.58	<0.001	0.42	0.25;0.72	0.001	0.45	0.33;0.62	<0.001	0.47	0.33;0.67	<0.001
Daily intake Tromsø7, n=2507†															
Protein, g/MJ	1.01	0.95;1.07	0.87	0.95	0.89;1.01	0.09				0.96	0.90;1.02	0.18			
Protein, g/kg BW	0.58	0.47;0.72	<0.001	0.57	0.46;0.72	<0.001	0.51	0.38;0.70	<0.001	0.54	0.43;0.67	<0.001	0.44	0.30;0.64	<0.001
Tracking of protein intake from Tromsø4 to Tromsø7, n=1908†															
Protein, g/MJ															
Stable high	1.00			1.00						1.00					
Stable low‡	0.67	0.48;0.92	0.02	0.84	0.60;1.18	0.32				0.80	0.57;1.14	0.22			
Decrease	0.80	0.58;1.10	0.17	0.91	0.65;1.26	0.57				0.89	0.64;1.24	0.49			
Increase	0.82	0.60;1.12	0.21	0.93	0.67;1.30	0.69				0.92	0.66;1.29	0.64			
Protein, g/kg BW															
Stable high	1.00			1.00			1.00			1.00			1.00		
Stable low‡	1.86	1.32;2.63	<0.001	1.96	1.38;2.78	<0.001	1.90	1.16;3.09	0.011	1.89	1.33;2.69	<0.001	1.63	1.09;2.44	0.02
Decrease	1.73	1.22;2.44	0.002	1.73	1.22;2.46	0.002	1.85	1.14;2.99	0.013	1.75	1.23;2.49	0.002	1.50	1.00;2.26	0.05
Increase	1.63	1.15;2.32	0.007	1.70	1.20;2.44	0.004	1.59	0.97;2.61	0.06	1.58	1.10;2.26	0.01	1.58	1.09;2.27	0.02

MJ: megajoule, BW: bodyweight. OR and 95% CI from logistic regression analyses. *N deviates slightly owing to a lack of data on specific variables. †Analytical sample for Model. ‡Low and medium tertiles. Model 1: Adjusted for baseline age. Model 2: Adjusted for baseline age, sex, smoking, education level and body mass index (not for analyses including protein in g/kg BW). Model 3: Model 2 + additionally adjusted for baseline energy intake (MJ/day). Model 4: Adjusted for Tromsø7 age, sex, smoking, comorbidity and body mass index (not for analyses with protein per g/kg BW). Model 5: Model 4 + additionally adjusted for Tromsø7 energy intake (MJ/day)

No significant associations were found between intake of protein relative to energy (in g/MJ) and pre-frailty/frailty.

In line with the observed beneficial effects of increased intake of protein expressed as g/kg BW on risk of pre-frailty/frailty as seen from longitudinal analyses, were findings reported by Beasley et al. in the Women's Health Initiative cohort (11). Beasley and colleagues found that a 20% increased intake of protein (g/kg BW) calibrated by 24-hour urinary nitrogen was associated with a 35% lower risk of frailty and a 22% lower risk of pre-frailty among 24,417 older women over a 3-year follow-up (11). In support of this, The Newcastle 85+ study showed that increased intake of protein in g/kg BW adjusted to normal BMI for older adults (22–27 kg/m^2) decreased the likelihood of transitioning from pre-frail to frail over five years in the oldest individuals (≥85 years) (15). Further, an American 10-year longitudinal study observed fewer health problems, including a study-specific definition of frailty, amongst community-dwelling women over 60 years with a daily protein intake >1.2 g/kg BW compared with those consuming <0.8 g/kg BW (14). The lower cut-off at 0.8 g/kg BW was set according to the current Recommended Daily Allowance for protein intended for healthy adults and older adults (42), and the upper cut-off (>1.2 g/kg BW) was set as emerging evidence has suggested that older adults need a higher protein intake to maintain muscle mass and function (14, 39, 43, 44). However, using these cut-offs (<0.8 and >1.2 g/kg BW), a prospective cohort study of Dutch adults (≥45 years) did not observe any association between protein intake and risk of frailty (19).

In line with our findings from cross-sectional analyses on intake of protein relative to BW, Rahi and colleagues (16) found that, in older French community-dwellers, daily protein intake ≥1 g/kg BW was significantly associated with a lower prevalence of frailty when compared with those consuming less protein. Conversely, Bollwein et al. (45) found no association between quartiles of protein intake (g/kg BW) and risk of frailty. Of note, the cross-sectional studies suffer the risk of reverse causality (46). The findings from supplementary analyses performed with imputed frailty data and on frailty score ≥2 and low grip strength emphasize the protective effect of consuming sufficient amounts of protein relative to one's BW.

The lack of association between intake of protein in g/MJ and risk of pre-frailty/frailty in this study, was somewhat confusing. However, the null findings observed in the longitudinal analyses are in agreement with Shikany et al. (20), who did not observe any association between quartiles of protein E% and frailty amongst older US men over a 4.6-year follow-up period. They did, however, show an inverse association between overall diet quality and risk of frailty. Furthermore, a Japanese prospective cohort found higher total protein intake to be negatively associated with pre-frailty/frailty development in older adults over 2 years; however, the results were no longer statistically significant after additional adjustment for energy intake. The authors suggested this indicated that increased energy intake mediated the contributions of protein intake towards reducing frailty development (47). This hypothesis was tested in our study by performing risk analyses stratified by quartiles of energy intake, however, this did not influence the results notably (data not

shown). Moreover, considering the observed higher BW and BMI of pre-frail/frail participants, it could be speculated that the observed increased risk of pre-frailty/frailty from intake of protein in g/kg BW is in fact due to differences in BW and body composition between groups, however, this was not investigated further due to lack of body composition data.

Contradictory to our findings, other studies have observed a relationship between energy-adjusted protein intake and frailty. Sandoval-Insausti and colleagues (12) found an inverse association between quartiles of total protein intake adjusted for energy and risk of frailty over 3.5 years amongst Spanish community-dwellers (≥60 years). The aforementioned findings of Beasley et al. of reduced risk of frailty with higher protein intake in g/kg BW persisted when calibrated protein intake was expressed as E% (11). In addition, two cross-sectional studies performed among community-dwelling older Italians (18) and Japanese women (17), respectively, found an inverse association between quintiles of daily intake of energy-adjusted protein and frailty.

Tracking of protein intake and risk of frailty

The low tracking values obtained in the present study are comparable with other tracking studies on lifestyle variables, and their magnitude is impaired by the variables' moderate reproducibility and the long follow-up period (48-50). For intake of protein expressed as g/kg BW, the observed opposing trends of patterns of protein intake between pre-frail/frail versus robust participants were not clearly reflected in the results, as all patterns of protein intake over time, except for a stable high intake, was associated with an increased risk of pre-frailty/frailty. However, the results from the sensitivity analyses indicate that a low or decreased level of intake is more crucial in terms of frailty risk than any pattern of increased protein intake. Most notably, tracking analyses on frailty score ≥2 and low grip strength should be interpreted with caution given the high level of uncertainty observed in the risk estimates.

Strengths and limitations

Major strengths of the current study are the prospective design, which allowed for follow-up of a large population-based sample over two decades, and the use of validated instruments to measure frailty components. Additionally, the assessment of the protein–frailty association in both longitudinal and cross-sectional analyses provides a more thorough understanding of the relationship than results from just one or the other.

A key limitation is that this study suffers from selective drop-out of participants with overall poorer health. This attrition contributes to the existing risk of selection bias associated with population-based studies, given that study participants tend to have both better health and higher socioeconomic status than non-participants (51). Non-attendance of the frailest individuals invited to Tromsø7 may have influenced the observed associations and contributed to the low observed prevalence of frailty. The observed prevalence was lower than reported in community dwellers worldwide (52), in Europe (53), and amongst participants ≥70 years in Tromsø5 in 2001 (54). In addition, missing frailty data might have contributed further to the low frailty prevalence. However, results from sensitivity analyses in participants with imputed frailty data, supported the main findings of an inverse association between intake of protein in g/kg BW and risk of pre-frailty/frailty.

Aside from the problem of selection bias, the relatively good health of the study participants may also reflect research showing that today's older adults are notably stronger than previous generations (55). Therefore, one could argue that Fried's cut-offs (3) are not optimal for identifying frailty accurately in the present study population, considering that these cut-offs are population-specific to older Americans in 2001.

This study suffers from the risk of misclassification given the combination of participants originally classified as pre-frail or frail in the more heterogeneous group 'pre-frail/frail' group and because the majority of participants in this group had a frailty score of 1. Consequently, there is a risk that practically healthy participants were grouped together with the genuinely frail. This was addressed to some extent in the results of the sensitivity analyses on frailty score ≥2, which for the most part supported the main results. Nonetheless, the majority of the pre-frail/frail participants were in fact pre-frail, and therefore comparisons with studies on frail participants are weakened.

Another important limitation is the risk of information bias introduced by self-reported variables, including the frailty criteria physical activity level, exhaustion and weight loss, and the dietary exposure variables and adjustment covariates. At both time points, the observed relative protein intake of the participants was in line with current Norwegian dietary recommendations for both healthy adults (0.8–1.5 g/kg BW, 10–20 E%) and older adults (1.1–1.3 g/kg BW, 15–20 E%) (39). However, the comparability of the protein estimates between the two surveys was reduced substantially because they were based on distinctly different questionnaires and dietary information, and different food composition databases were used for the protein calculations. The estimated nutritional intake in Tromsø7 was based on a much higher number of dietary items than in Tromsø4, and it is natural to assume that the reported intake will increase with increased number of foods asked about. Additionally, portion sizes in Tromsø4 were estimated on the basis of previous dietary surveys whereas they were specifically asked for in the Tromsø7 FFQ. Therefore, there is a risk that the observed increased daily intake of protein over time may be attributable to methodological differences.

The two relative protein variables measured in this study have different sources of error according to their respective adjustment variables, given that BW was measured objectively whilst estimated energy intake was based on self-reported data. Moreover, the protein variables reflect the participants' protein intake in two different ways. By adjusting for energy, one can to a certain extent reduce the confounding effect of energy in the analyses, and account for the influence of other factors that affect energy intake, such as physical activity level, body composition, and metabolism (56). On the other hand, changes in BW may themselves influence protein intake in g/kg BW.

Therefore, observed changes in intake of protein in g/kg BW may be explained either by changes in protein intake, BW or both.

Unfortunately, there is no validation study on the nutritional data obtained from Tromsø4, but the estimated proportions of energy obtained from macronutrients were comparable to data in the first two Norkost surveys (1994–95, 1997), intended to be representative of the Norwegian population aged 16–79 years (24, 57). The much more comprehensive FFQ used in Tromsø7 has been validated (58-60) and is considered a suitable tool for dietary assessment in large population surveys.

In addition to being self-reported, the majority of the study covariates were dichotomized which led to loss of information and potential for residual confounding. The findings from the present study are generalizable to community-dwelling Norwegian adults and older adults, as long as these limitations are kept in mind. Specifically, the generalizability of the results from the tracking analyses is impaired by the use of study-specific measures as opposed to objective cut-offs for protein intake (50).

One further limitation of the study is that there are no repeated measurements of frailty. However, no information on frailty status was available at baseline. Similarly, repeated measurements of protein intake between Tromsø4 and Tromsø7 might have added to the study but no such data were available. There were also no data available to assess the influence of different sources of protein (plant versus animal), the amount of protein intake per meal, and the timing of protein intake.

In conclusion, the vast majority of the pre-frail/frail participants in this population-based study were pre-frail. The results highlight the significant associations between protein intake, BW and frailty development, particularly via the transitional state of pre-frailty. These findings emphasize the importance of consuming an adequate amount of protein in adulthood and of complying with current dietary recommendations in order to prevent age-related loss of muscle mass and function.

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Supplementary files

Supplementary Table 1.

Modifications of the frailty phenotype in the Tromsø7 Study 2015-16

	Criteria for frailty by Fried et al. 2001	**Criteria for frailty in Tromsø7**
Weight loss	Self-reported, from the question "In the last year, have you lost more than 10 pounds unintentionally (i.e., not due to dieting or exercise)?". If yes, then frail for weight loss criterion. Or, measured at follow up: ≥5% unintentional loss of body weight in prior year (by direct measurement of weight at follow-up). Weight loss calculated as: (Weight in previous year – current measured weight)/(weight in previous year) = K. If K ≥0.05 and the subject does not report to have been trying to lose weight, then frail for weight loss = Yes.	Self-reported, based on a question from the Malnutrition Universal Screening Tool: "Have you involuntary lost weight during the last 6 months?". If yes, then frail for the weight loss criterion.
Exhaustion	Self-reported, based on two questions from the Center for Epidemiologic Studies Depression Scale: (a) I felt that everything I did was an effort (b) I could not get going. "How often in the last week did you feel this way?" 0 = rarely or none of the time (<1 day) 1 = some or a little of the time (1–2 days) 2 = a moderate amount of the time (3–4 days) 3 = most of the time. Answer 2 or 3 to either of these questions led to categorization as frail for the exhaustion criterion.	Self-reported, based on the Hopkins Symptoms Checklist 10: "Have you experienced any of this the last week: That everything is a struggle?" 1 = No complaint 2 = Little complaint 3 = Pretty much 4 = Very much Answer 3 or 4 led to categorization as frail by the exhaustion criterion.
Physical activity	Self-reported, based on Minnesota Leisure Time Activity short questionnaire asking about walking, chores (moderately strenuous), mowing the lawn, raking, gardening, hiking, jogging, biking, exercise cycling, dancing, aerobics, bowling, golf, singles tennis, doubles tennis, racquetball, calisthenics, swimming. Kcals per week expended are calculated using standardized algorithm. The lowest 20% was identified for each sex. *Frailty cut-off for physical activity:* *Men*: <383 kcal of physical activity per week *Women*: <270 kcal of physical activity per week	Self-reported, based on Saltin & Grimby's Physical Activity Level Scale: Describe your exercise and physical exertion in leisure time over the last year: 1 = Reading, watching TV/screen or other sedentary activity? 2 = Walking, cycling or other forms of exercise at least 4 hours a week? 3 = Participation in recreational sports, heavy gardening, snow shovelling etc. at least 4 hours a week? Answer 1 led to categorization as frail for the physical activity criterion.

Walking speed	Time to Walk (s) 15 feet at usual pace. Stratified by sex and height (gender-specific cut-off at medium height). Lowest 20% were identified, resulting in the following cut-off for the walking speed criterion of frailty:		Short Physical Performance Battery walking test: Fastest (s) of two times to walk 4 m on average pace. Stratified by sex and height. Calculated from s/4 m to s/15 feet (4.572 m)for adaption to Fried's criteria: *(s/4m)*1.143=s/4.572m*	
	Men Height ≤173 cm Height >173 cm	*Cut-off (s):* ≥7 seconds ≥6 seconds	*Men* Height ≤173 cm Height >173 cm	*Cut-off (s):* ≥7 seconds ≥6 seconds
	Women Height ≤159 cm Height >159 cm	*Cut-off (s):* ≥7 seconds ≥6 seconds	*Women* Height ≤159 cm Height >159 cm	*Cut-off (s):* ≥7 seconds ≥6 seconds
Grip strength	Measured by Jamar dynamometer (kg), maximal strength of three trials in dominant hand. Stratified by sex and BMI quartiles. Lowest 20% were identified, resulting in the following cut-off for frailty:		Measured by Jamar dynamometer (kg), maximal of three trials in each hand (6 measurements). Stratified by sex and BMI quartiles.	
	Men BMI <24 BMI 24.1–26 BMI 26.1–28 BMI >28	*Cut-off (kg):* <29 kg <30 kg <30 kg <32 kg	*Men* BMI <24 BMI 24.1–26 BMI 26.1–28 BMI >28	*Cut-off (kg):* <29 kg <30 kg <30 kg <32 kg
	Women BMI <23 BMI 23.1–26 BMI 26.1–29 BMI >29	*Cut-off (kg):* <17 kg <17.3 kg ≤18 kg ≤21 kg	*Women* BMI <23 BMI 23.1–26 BMI 26.1–29 BMI >29	*Cut-off (kg):* <17 kg <17.3 kg ≤18 kg ≤21 kg
Frailty score	0 = Not frail/robust 1–2 = Intermediate/pre-frail ≥3 = Frail		0 = Not frail/robust 1–2 = Intermediate/pre-frail ≥3 = Frail	
Pre-frailty/frailty score			0 = Not frail/robust ≥1 = Pre-frail/frail	

Supplementary Table 2

Follow-up characteristics of men and women by frailty status in Tromsø7 (n=3726)

	All (n=3726)			Women (n=1906)			Men (n=1820)		
Follow-up characteristics	**Robust (n=2681)**	**Pre-frail/frail (n=1045)**	**P***	**Robust (n=1343)**	**Pre-frail/ frail (n=563)**	**P***	**Robust (n=1338)**	**Pre-frail/ frail (n=482)**	**P***
Attendees, %	72.0	28.0		70.5	29.5		73.5	26.5	
Age (years), mean (sd)	71.9 (4.9)	73.3 (5.6)	<0.001	71.6 (4.9)	73.2 (5.6)	<0.001	72.1 (4.9)	73.4 (5.6)	<0.001
Weight (kg), mean (sd)	77.2 (13.8)	79.0 (16.3)	0.001	70.4 (12)	73.4 (15)	<0.001	84.1 (12)	85.5 (15)	0.04
Height (cm), mean (sd)	169 (9.0)	167 (9.6)	<0.001	162 (5.9)	161 (6.6)	<0.001	176 (6.2)	175 (6.9)	0.01
BMI (kg/m^2), mean (sd)	27.0 (3.9)	28.2 (5.0)	<0.001	26.7 (4.4)	28.3 (5.6)	<0.001	27.3 (3.4)	28.0 (4.4)	<0.001
Daily smoking, n (%)	2651 (100)	1032 (100)		1324 (100)	554 (100)		1327 (100)	478 (100)	
Currently, n (%)	215 (8.1)	157 (15.2)	<0.001	188 (8.9)	85 (15.3)	<0.001	97 (7.3)	72 (15.1)	<0.001
Previously, n (%)	1417 (53.5)	533 (51.7)		632 (47.7)	258 (46.6)		785 (59.2)	275 (57.5)	
Never, n (%)	1019 (38.4)	342 (33.1)		574 (43.4)	211 (38.1)		445 (33.5)	131 (27.4)	
Married or cohabitation, n (%)	1958 (76.0)	726 (73.6)	0.12	832 (65.7)	341 (65.7)	0.99	1126 (86.1)	385 (82.3)	0.05
Education†, n (%)	2613 (100)	1010 (100)		1309 (100)	545 (100)		1304 (100)	465 (100)	
Primary/partly secondary, n (%)	973 (37.2)	477 (47.2)		568 (43.4)	313 (57.4)		405 (31.1)	164 (35.3)	
Upper secondary, n (%)	709 (27.1)	269 (26.6)	<0.001	332 (25.3)	130 (23.9)	<0.001	377 (28.9)	139 (29.9)	0.14
Short tertiary, n (%)	434 (16.6)	133 (13.2)		162 (12.4)	41 (7.5)		272 (20.9)	92 (19.8)	
Short tertiary, n (%)	497 (19.0)	131 (13.0)		247 (18.9)	61 (11.2)		250 (19.2)	70 (15.0)	
Social support‡, n (%)	2363 (90.9)	864 (85.4)	<0.001	1168 (90.3)	447 (82.8)	<0.001	1195 (91.5)	417 (88.4)	0.04
Good self-perceived health, n (%)	1868 (70.6)	460 (44.6)	<0.001	920 (69.7)	227 (41.1)	<0.001	948 (71.4)	233 (48.6)	<0.001
Physically active, n (%)	2536 (100)§	452 (45.5)	<0.001	1249 (100)§	245 (47.1)	<0.001	1287 (100)§	207 (43.7)	<0.001
High alcohol consumption‖, n (%)	617 (25.4)	165 (17.6)	<0.001	360 (29.3)	90 (17.4)	<0.001	257 (21.4)	75 (17.7)	0.11
Comorbidity, n (%)	334 (12.6)	219 (21.2)	<0.001	126 (9.6)	89 (16.1)	<0.001	208 (15.6)	130 (27.1)	<0.001
Coronary heart disease{, n (%)	544 (20.8)	287 (28.3)	<0.001	175 (13.5)	114 (21.0)	<0.001	369 (27.8)	173 (36.6)	<0.001
Pulmonary disease#, n (%)	370 (14.2)	192 (18.9)	<0.001	203 (15.8)	113 (20.8)	0.01	167 (12.7)	79 (16.7)	0.03
Cancer, n (%)	404 (15.6)	195 (19.4)	0.01	190 (14.8)	89 (16.7)	0.31	214 (16.4)	106 (22.4)	0.003
Stroke, n (%)	129 (5.0)	74 (7.4)	0.01	41 (3.2)	25 (4.7)	0.12	88 (6.8)	49 (10.5)	0.01
Diabetes, n (%)	185 (7.1)	136 (13.7)	<0.001	80 (6.2)	64 (12.0)	<0.001	105 (8.0)	72 (15.6)	<0.001

sd: standard deviation, BMI: body mass index, MJ: megajoule. N deviates slightly owing to a lack of data on specific variables. [*]P-value from Student's t-test for continuous variables and chi-square test for categorical variables between pre-frail/frail and robust women and men. [†]Primary/secondary school <10 years; upper secondary education (min. 3 years); college/university <4 years; college/university ≥4 years. [‡]Self-reported satisfactory number of good friends. [§]Included in the frailty criteria; all inactive participants are classified as pre-frail/frail. [‖]Daily alcohol intake >10 g (women) or 20 g (men). [{]Angina pectoris, myocardial infarction, heart failure and/or atrial fibrillation. [#]Asthma and/or chronic bronchitis/emphysema.

Supplementary Table 3

Frailty status by age groups in Tromsø7 (n=3726)

	All (n=3726)				Women (n=1906)			Men (n=1820)		
Age (years) in Tromsø7	**Robust (n=2681)**	**Pre-frail (n=1009)**	**Frail (n=36)**	**P***	**Robust (n=1343)**	**Pre-frail (n=537)**	**Frail (n=26)**	**Robust (n=1338)**	**Pre-frail (n=472)**	**Frail (n=10)**
66–69, n=1397†	1060 (75.7)	329 (23.6)	8 (0.6)		570 (75.8)	175 (23.3)	7 (0.9)	490 (76.0)	154 (23.9)	1 (0.2)
70–79, n=1925†	1381 (71.7)	521 (27.1)	23 (1.2)	<0.001	656 (68.9)	279 (29.3)	17 (1.8)	725 (74.5)	242 (24.9)	6 (0.6)
≥80, n=404†	240 (59.4)	159 (39.4)	5 (1.2)		117 (57.9)	83 (41.1)	2 (1.0)‡	123 (60.9)	76 (37.6)	3 (1.5)‡

*P-value from Fisher's exact test between age groups and frailty status. †N for men and women combined. ‡No tests performed owing to low n (<5) in cell.

Supplementary Table 4

Baseline characteristics of participants in Tromsø4 by Tromsø7 participation status (n=10745)

	Did not attend Tromsø7 (n=5990)	Attended Tromsø7 (n=4755)	P*
Attendees, %†	55.8	44.2	
Women, n (%)	2968 (49.6)	2493 (52.4)	0.003
Age (years), mean (sd)	57.3 (7.5)	51.8 (5.5)	<0.001
Weight (kg), mean (sd)	74.7 (14)	74.2 (13)	0.13
Height (cm), mean (sd)	169 (9.4)	170 (9.1)	<0.001
BMI (kg/m^2), mean (sd)	26.1 (4.2)	25.7 (3.5)	<0.001
Physically active, n (%)	3396 (56.8)	3108 (65.4)	<0.001
Comorbidity, n (%)	425 (7.1)	105 (2.2)	<0.001
Daily nutrient intake			
N (%)	3304 (50.0)	3303 (50.0)	
Protein (g), mean (sd)	78.7 (21)	77.8 (21)	0.07
Protein (g/MJ), mean (sd)	10.2 (1.4)	10.0 (1.3)	<0.001
Protein (g/kg BW), mean (sd)	1.07 (0.3)	1.07 (0.3)	0.25
Energy (MJ), mean (sd)	7.8 (2.2)	7.9 (2.2)	0.29

sd: standard deviation, BMI: body mass index, MJ: megajoule, BW: bodyweight. N deviates slightly owing to a lack of data on specific variables. *P-value by Student's t-test for continuous variables and chi-square test for categorical variables. †Participated in Tromsø4.

Supplementary Table 5

Odds ratios (OR) and 95% confidence intervals (CI) for daily intakes of protein in Tromsø4 and pre-frailty/frailty adjusted for Tromsø7 protein intake (n=1908)

Dietary exposure	Model 6 (n=1902)			Model 7 (n=1881)		
	OR	95% CI	P	OR	95% CI	P
Daily intake Tromsø4						
Protein, g/MJ	1.01	0.93;1.10	0.86	1.01	0.93;1.11	0.75
Protein, g/kg BW	0.52	0.33;.082	0.005	0.61	0.39;0.95	0.03

MJ: megajoule, BW: bodyweight. OR and 95% CI from logistic regression analyses. Analyses performed in participants included in tracking analyses, i.e. with data on estimated protein intake from both Tromsø4 and Tromsø7. Model 6: Adjusted for Tromsø4 age, sex, smoking, education level and body mass index (not for analysis including protein in g/kg BW) plus Tromsø7 protein intake. Model 7: Adjusted for age, sex and Tromsø7 smoking status, comorbidity and body mass index (not for analysis including protein in g/kg BW) plus Tromsø7 protein intake.

Supplementary Table 6

Odds ratios (OR) and 95% confidence intervals (CI) for daily intakes of protein in Tromsø4, and Tromsø7, tracking of protein intake from Tromsø4 to Tromsø7, and pre-frailty/frailty in Tromsø7 in participants with different levels of imputed frailty data* (n=3726)

Dietary exposure	25% imputation†			50% imputation†			75% imputation†			100% imputation†		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Daily intake Tromsø4, n=3089‡												
Protein, g/MJ	1.02	0.96;1.08	0.58	1.01	0.95;1.07	0.79	1.01	0.96;1.07	0.67	1.00	0.95;1.06	0.99
Protein, g/kg BW	0.46	0.35;0.62	<0.001	0.52	0.40;0.70	<0.001	0.61	0.46;0.81	<0.001	0.75	0.57;0.99	0.04
Daily intake Tromsø7, n=2507‡												
Protein, g/MJ	0.95	0.90;1.01	0.10	0.95	0.89;1.00	0.06	0.95	0.90;1.01	0.08	0.95	0.90;1.01	0.08
Protein, g/kg BW	0.65	0.53;0.79	<0.001	0.66	0.54;0.80	<0.001	0.65	0.53;0.78	<0.001	0.65	0.53;0.78	<0.001
Tracking of protein intake from Tromsø4 to Tromsø7, n=1908‡												
Protein, g/MJ												
Stable high	1.00			1.00			1.00			1.00		
Stable low§	0.87	0.63;1.20	0.40	0.96	0.70;1.30	0.77	0.98	0.72;1.32	0.88	0.98	0.72;1.32	0.88
Decrease	0.93	0.68;1.28	0.66	0.93	0.68;1.25	0.62	0.94	0.70;1.26	0.66	0.94	0.70;1.26	0.66
Increase	0.89	0.65;1.22	0.47	0.87	0.65;1.18	0.38	0.90	0.67;1.21	0.48	0.90	0.67;1.21	0.48
Protein, g/kg BW												
Stable high	1.00			1.00			1.00			1.00		
Stable low§	1.86	1.35;2.58	<0.001	1.81	1.33;2.47	<0.001	1.75	1.31;2.35	<0.001	1.75	1.31;2.35	<0.001
Decrease	1.64	1.18;2-27	0.003	1.55	1.14;2.11	0.006	1.40	1.04;1.87	0.03	1.40	1.04;1.87	0.03
Increase	1.58	1.13;2.21	0.007	1.48	1.08;2.03	0.014	1.32	0.98;1-78	0.07	1.32	0.98;1.78	0.07

MJ: megajoule, BW: bodyweight. OR and 95% CI from logistic regression analyses. *Frailty was imputed in individual frailty items in robust participants with missing frailty data (n=910). †Robust participants with missing frailty data: 25% (n=228), 50% (n=455), 75% (n=683), 100% (n=910). ‡Analytical sample for Model. §Low and medium tertiles. Model 2: Adjusted for baseline age, sex, smoking, education level and body mass index (not for analyses including protein in g/kg BW).

Supplementary Table 7

Odds ratios (OR) and 95% confidence intervals (CI) for daily intakes of protein in Tromsø4, and Tromsø7, tracking patterns of protein intake from Tromsø4-Tromsø7, and frailty score ≥2 in Tromsø7 (n=2857)

Dietary exposure	**Model 1**			**Model 2***		
	OR	**95% CI**	**P**	**OR**	**95% CI**	**P**
Daily intake Tromsø4, n=2371†						
Protein, 10 g/MJ	1.00	0.88;1.14	0.95	0.92	0.80;1.05	0.21
Protein, g/kg BW	0.23	0.12;0.47	<0.001	0.26	0.13;0.53	<0.001
Daily intake Tromsø7, n=1939†						
Protein, 10 g/MJ	1.06	0.92;1.21	0.45	0.96	0.83;1.11	0.61
Protein, g/kg BW	0.56	0.33;0.92	0.02	0.51	0.31;0.85	0.009
Tracking of protein intake from Tromsø4 to Tromsø7, n=1482†						
Protein, g/MJ						
Stable high	1.00			1.00		
Stable low‡	0.86	0.41;1.79	0.68	1.44	0.65;3.18	0.37
Decrease	0.89	0.43;1.85	0.76	1.19	0.55;2.58	0.66
Increase	0.97	0.47;2.01	0.94	1.42	0.65;3.08	0.38
Protein, g/kg BW						
Stable high	1.00			1.00		
Stable low‡	2.21	1.02;4.80	0.04	2.51	1.14;5.51	0.02
Decrease	1.49	0.67;3.34	0.33	1.68	0.74;3.81	0.22
Increase	1.82	0.82;4.05	0.14	1.82	0.80;4.10	0.15

MJ: megajoule, BW: bodyweight. OR and 95% CI from logistic regression analyses. Analyses performed in participants with frailty scores 0, 2, 3. *N deviates slightly owing to a lack of data on specific variables. †Analytical sample for Model. ‡Low and medium tertiles. Model 1: Adjusted for baseline age. Model 2: Adjusted for baseline age, sex, smoking, education level and body mass index (not for analyses including protein in g/kg BW).

Supplementary Table 8

Odds ratios (OR) and 95% confidence intervals (CI) for daily intakes of protein in Tromsø4, and Tromsø7, tracking patterns of protein intake from Tromsø4 to Tromsø7, and low grip strength in Tromsø7 (n=2774)

Dietary exposure	**Model 1**			**Model 2***		
	OR	**95% CI**	**P**	**OR**	**95% CI**	**P**
Daily intake Tromsø4 , n=2258†						
Protein, gMJ	1.06	0.93;1.20	0.37	0.99	0.87;1.14	0.88
Protein, g/kg BW	0.58	0.30;1.13	0.11	0.74	0.37;1.47	0.37
Daily intake Tromsø7, n=1995†						
Protein, gMJ	1.09	0.96;1.24	0.19	1.04	0.91;1.18	0.58
Protein, g/kg BW	0.48	0.30;0.79	0.004	0.45	0.28;0.73	0.001
Tracking of protein intake from Tromsø4 to Tromsø7, n=1507†						
Protein, gMJ						
Stable high	1.00			1.00		
Stable low‡	0.95	0.47;1.94	0.89	1.19	0.57;2.47	0.65
Decrease	0.83	0.41;1.69	0.61	0.84	0.40;1.74	0.64
Increase	1.05	0.53;2.09	0.89	1.25	0.62;2.53	0.53
Protein, g/kg BW						
Stable high	1.00			1.00		
Stable low‡	1.54	0.66;3.59	0.31	1.58	0.67;3.72	0.29
Decrease	2.25	1.01;4.98	0.05	2.74	1.22;6.17	0.02
Increase	1.96	0.86;4.42	0.11	1.82	0.79;4.19	0.16

MJ: megajoule, BW: bodyweight. OR and 95% CI from logistic regression analyses. *N deviates slightly owing to a lack of data on specific variables. †Analytical sample for Model. ‡Low and medium tertiles. Model 1: Adjusted for baseline age. Model 2: Adjusted for baseline age, sex, smoking, education level and body mass index (not for analyses including protein in g/kg BW).

Paper II

II

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Fish intake and pre-frailty in Norwegian older adults - a prospective cohort study: the Tromsø Study 1994–2016

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Abstract

Background Pre-frailty is an intermediate, potentially reversible state before the onset of frailty. Healthy dietary choices may prevent pre-frailty. Fish is included in most healthy diets, but little is known about the association between long-term habitual fish intake and pre-frailty. We aimed to elucidate the longitudinal association between the frequency of fish intake and pre-frailty in a cohort of older adults in Norway.

Methods 4350 participants (52% women, ≥65 years at follow-up) were included in this prospective cohort study. Data was obtained from three waves of the population-based Tromsø Study in Norway; Tromsø4 (1994–1995), Tromsø6 (2007–2008) and Tromsø7 (follow-up, 2015–2016). Frailty status at follow-up was defined by a modified version of Fried's phenotype. Fish intake was self-reported in the three surveys and assessed as three levels of frequency of intake: low (0–3 times/month), medium (1–3 times/week) and high (≥4 times/week). The fish–pre-frailty association was analysed using multivariable logistic regression in two ways; (1) frequency of intake of lean, fatty and total fish in Tromsø6 and pre-frailty at follow-up, and (2) patterns of total fish intake across the three surveys and pre-frailty at follow-up.

Results At follow-up, 28% ($n=1124$) were pre-frail. Participants with a higher frequency of lean, fatty and total fish intake had 28% (odds ratio (OR) = 0.72, 95% confidence interval (CI) = 0.53, 0.97), 37% (OR = 0.63, 95% CI = 0.43, 0.91) and 31% (OR = 0.69, 95% CI = 0.52, 0.91) lower odds of pre-frailty 8 years later compared with those with a low intake, respectively. A pattern of stable high fish intake over 21 years was associated with 41% (OR = 0.59, 95% CI = 0.38, 0.91) lower odds of pre-frailty compared with a stable low intake.

Conclusions A higher frequency of intake of lean, fatty and total fish, and a pattern of consistent frequent fish intake over time, were associated with lower odds of pre-frailty in older community-dwelling Norwegian adults. These results emphasise the important role of fish in a healthy diet and that a frequent fish intake should be promoted to facilitate healthy ageing.

Keywords Ageing, Diet, Epidemiology, Fish, Pre-frailty, Geriatrics

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Background

A key focus in ageing research is the frailty syndrome [1]. Frailty is a transitional state between healthy ageing and disability in older adults, and frailty prevention is significantly important at both societal and individual level [2]. Frail individuals are less resilient to trauma and stress and more prone to adverse outcomes than non-frail individuals of the same chronological age [3, 4].

Physical frailty has been defined by Fried et al. by the following five characteristics: exhaustion, unintentional weight loss, low physical activity, slowness and weakness [5]. The presence of three or more of these characteristics classifies individuals as frail, whereas the presence of one or two classifies individuals as pre-frail, an intermediate state with an elevated risk of progression to frailty [4–7]. Frailty is a dynamic syndrome and, therefore, pre-frailty and frailty are potentially reversible [6, 8]. The importance of early interventions has been emphasized and, specifically, the pre-frail state has been identified as a suitable target for preventive measures [4, 8].

Research suggests that there is an association between a healthy diet and lower risk of frailty in older adults [9–11]. The vast majority of existing studies focus on frailty rather than pre-frailty, but a recently published systematic review and meta-analysis found that a higher adherence to the Mediterranean diet [12] was associated with lower risk of pre-frailty [13]. Fish is a food group that is often included in healthy diets [14–16], like the Mediterranean diet [12] and is a rich source of several nutrients associated with good overall health [14, 17]. Two reviews suggested that fish, and nutrients through which fish is an important dietary source, prevented physical frailty and its individual characteristics [18, 19]. Fish is typically classified based on fat content (fatty vs lean) or the colour of the meat (red vs white). Both methods cover all fish types as white fish can be both fatty (halibut) and lean (cod), and vice versa. As the nutrient composition of lean and fatty fish differs, a healthy diet should include both [20].

Findings from longitudinal, cross-sectional and intervention studies indicate that intake of fish is associated with beneficial health effects in older adults, including healthier ageing [21], reduced risk of frailty [22–24], increased grip strength [25] and improved muscle mass and function [26]. However, results are inconsistent, and no study has specifically investigated the association between different patterns of habitual fish intake and later health outcomes.

The Norwegian dietary guidelines recommend eating fish for dinner two to three times a week and to choose fish as a spread or topping on bread [20]. With its long coastal area and longstanding fishing tradition, fish intake in Norway has traditionally been high compared with other countries [27, 28]. This is especially true for Northern Norway, where fishing has been, and still is, an important part of everyday life [28–30]. Therefore, older individuals from Northern Norway provide a suitable cohort for studying the relationship between fish intake and health-related outcomes.

There are few longitudinal studies on fish intake and pre-frailty [22, 23]. We hypothesize that a frequent fish intake is associated with lower risk of pre-frailty, and that maintaining a high frequency of intake over time reflects some consistency in healthy eating habits which will consequently reduce the risk of pre-frailty. Therefore, building on our previous research on nutrition and pre-frailty/frailty [31], we aimed to elucidate the longitudinal association between fish intake and pre-frailty in an older northern Norwegian, population-based cohort. First, we investigated the association between frequency of intake of lean, fatty and total fish and pre-frailty 8 years later – a follow-up period that we considered to be clinically relevant in terms of a possible implementation of preventive measures. Second, to assess the influence of long-term consistent fish intakes, we investigated the association between consistent low, medium, and high frequency of total fish intake over 21 years and pre-frailty.

Methods

The Tromsø Study

The Tromsø Study, described in detail elsewhere [32, 33] is a large population-based study consisting of seven surveys (Tromsø1 to Tromsø7) conducted between 1974 and 2016. Based on the official population registry, total birth cohorts and random samples of residents of the municipality of Tromsø in Northern Norway were invited. In total, 45 473 men and women have participated in one or more surveys [33]. Invitations were sent by mail together with a short questionnaire. On attendance (visit 1), the participants received more comprehensive questionnaires and underwent biological sampling and clinical examinations. A subsample (predefined before study start, but only invited if the person attended visit 1) attended additional clinical examinations (visit 2).

Study population

We used data from Tromsø4 (1994–1995), Tromsø6 (2007–2008, baseline survey for main analysis) and Tromsø7 (2015–2016, follow-up survey). Tromsø4 included 27 158 participants (attendance 77%), aged 25–97 [34]. Owing to age-specific questionnaires in Tromsø4, only data from participants aged < 70 years were used in the present study [34]. Tromsø6 included 12 977 participants (66% attendance), aged 30–87 [35].

Tromsø7 included 21 083 participants (65% attendance), aged 40–99 [33].

For the main analysis, baseline was set to Tromsø6 with 8-year follow-up at Tromsø7 (Fig. 1). To ensure an eligible and reliable study sample of appropriate age at follow-up (≥65 years), we excluded those younger than 57 years at baseline, those with a Mini-Mental State Examination (MMSE) score < 24, and those with no data on baseline frequency of fish intake. Of the 6837 eligible participants, 4409 also participated at follow-up. At follow-up, we excluded those without any frailty data ($n=17$) and - given the low prevalence - those classified as frail ($n=42$), leaving 4350 participants for the main analysis. Among these, a subsample of 3229 participants with complete data on fish intake in all three surveys (Tromsø4, Tromsø6 and Tromsø7) was identified for tracking analysis of patterns of fish intake over 21 years (Fig. 1). For clarity, we will refer to the subsamples as 'main sample' ($n=4350$) and 'tracking sample' ($n=3229$) to distinguish between the two.

Dietary assessment

Fish intake in all surveys was based on two questions about frequency of intake of lean (e.g., cod, saithe) and fatty (e.g., salmon, trout, mackerel, herring, halibut) fish with answer alternatives ranging from '0–1 times a month' to '1–2 times a day' [36–38] (Table S1). The exact wording of the questions and answers differed slightly across the surveys. To ensure a sufficient number of participants and thus statistical power to perform analyses on the different frequencies of fish intake, the lowest frequency category was merged with the second lowest ('0–1 times a month' plus '2–3 times a month'), and the highest frequency category was merged with the second highest ('4–6 times a week' plus '1–2 times a day'). This resulted in three levels of fish intake: '0–3 times a month' (low), '1–3 times a week' (medium) and '≥4 times a week' (high) (Table S1). Total fish intake was estimated by combining frequencies of lean and fatty fish intake. Each frequency interval of lean and fatty fish intake was quantified as total weekly frequency of fish intake (x/week), summed together, and then transformed back into the original frequency intervals ('categories') of fish intake.

For assessment of total fish intake over time, stable (low, medium, high) or inconsistent patterns were identified (Table 2). Stable patterns were identified as the same reported frequency of intake in all three surveys (e.g., low, low, low), or two similar frequencies of intake plus one frequency of intake differing by one level. For example, the combination 'low', 'medium', 'low' frequency of intake was also considered a stable low pattern. The remaining patterns were intakes that spread across the three levels

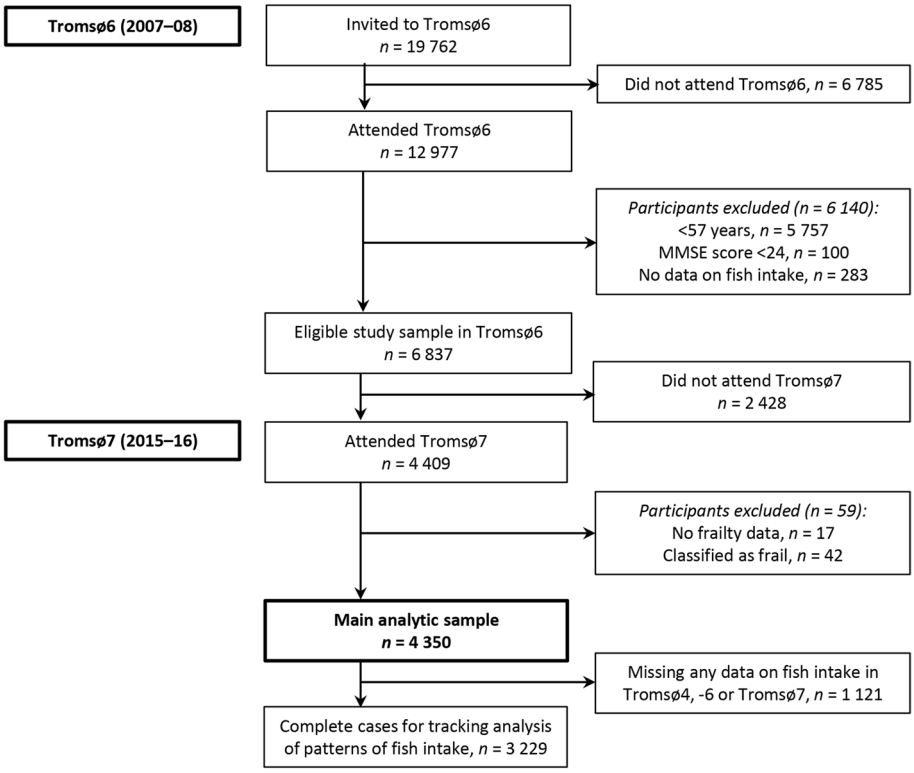

Fig. 1 Flow chart of the study population

of frequency of intake (e.g., low, high, low), and were classified as inconsistent patterns.

Frailty assessment

In Tromsø6 and at follow-up, a modified versions of Fried's physical frailty phenotype (Table S2) was used to categorize participants as frail, pre-frail, or robust. Frailty in Tromsø4 was not defined as data were insufficient.

At follow-up, weight loss was defined as answer 'yes' to the question: 'Have you involuntarily lost weight during the last 6 months?'. Low physical activity was defined as the lowest category ('Mainly reading, watching TV/screen or other sedentary activity') in the Saltin–Grimby questionnaire [39]. Exhaustion was defined as either of the two highest categories ('Pretty much' or 'Very much') to the question 'Have you felt that everything is a struggle during the last week?', from the Hopkins Symptoms Checklist 10 [40]. Low grip strength and slow walking speed were measured at visit 2 and defined using sex-specific cut-offs, further stratified by body mass index (BMI) quartiles and medium height, respectively, as originally proposed by Fried et al. [5]. BMI was calculated as body weight (kg) divided by height (m) squared (kg/m^2). Grip strength (kg) was measured using an electric Jamar (PLUS+) dynamometer [33]. The strongest of six measurements was recorded according to the Southampton protocol [41]. Walking speed was assessed by the Short Physical Performance Battery test [42] where participants walked 4 m at their average speed twice. The fastest test was recalculated to seconds per 15 feet to match Fried's original definition [5].

Frailty was defined in the same way in Tromsø6, except without the walking speed characteristic owing to lack of information. Additionally, grip strength in bar was measured using a Martin-Vigorimeter. Values in bar were calculated to kilopascal before converted to kg using sex-specific conversion factors (women: 2.43, men: 1.68), as according to Neumann et al. [43] to fit Fried's cut-offs [5]. All characteristics were dichotomised. Participants with none of these characteristics were classified as robust, participants with one or two present were classified as pre-frail, and those with three or more characteristics were classified as frail.

Covariates

Covariates were selected based on empirical knowledge on relevant confounders between diet and pre-frailty. In Tromsø4, body weight (kg) and height (cm) were measure with light clothing and no shoes on an electronic scale. Married/cohabitation included self-reported marriage/partnership/living with spouse/partner. Social support was defined as a yes to the question 'Do you feel like you have enough good friends?'. Good self-rated health was defined as the two highest ('Good' and 'Very good') out of five categories to the question 'What is your current state of health?'. Self-reported smoking status was never, former or daily smoker. Self-reported education level was grouped into primary/lower secondary school ($\leq$10 years), upper secondary school and higher education (college/university). Self-reported physical activity level was defined as low if $<$3 h per week of 'Light exercise without sweating/being out of breath'. High alcohol intake was defined as an estimated daily intake of $\geq$10 g for women and $\geq$20 g for men, as the Norwegian Directorate of Health advises against intakes above this [44]. Daily alcohol intake was estimated based on self-reported frequency and average units of alcohol consumed. Comorbidity was defined by two or more of the major non-communicable diseases (previous and/or current): cardiovascular disease (angina pectoris, myocardial infarction, stroke), chronic respiratory diseases (chronic bronchitis, asthma), diabetes and cancer. All diseases were self-reported, except cancer, which was obtained from the Norwegian Cancer Registry.

These characteristics were collected in the same way in Tromsø6, with some exceptions; self-reported low physical activity level was defined as the lowest category in the already mentioned Saltin–Grimby questionnaire [39]; alcohol intake was calculated based on the self-reported frequency and average units of alcohol consumed using the first two questions in the Alcohol Use Disorder Identification Test [45]. At visit 2, cognitive function was assessed via the MMSE using a cut-off for normal cognitive function at score 24, which is validated and commonly used for community-dwelling older adults [46].

Statistical analysis

Characteristics and frequencies of fish intake at different time points are presented as means and counts for the total sample and stratified by follow-up frailty status (Tables 1 and 2). Differences between robust and pre-frail groups were tested using the chi-square test for categorical variables, Student's *t*-test for continuous variables and Cochran-Armitage test for trend across frequencies of fish intake. Continuous variables were graphically inspected for normality.

The longitudinal association between frequency of fish intake and pre-frailty was analysed via multivariable logistic regression in two ways: first, the association between frequency of intake of lean, fatty and total fish in Tromsø6 and pre-frailty 8 years later (Table 3). Three multivariable logistic regression models were run, adjusted for relevant Tromsø6 confounders. Model 1 was adjusted for age and sex. Model 2 was additionally adjusted for BMI, education, smoking, physical activity, self-reported health and comorbidity. In addition, to

Table 1 Baseline characteristics and fish intake of main study sample ($n=4350$)

Baseline characteristics in Tromsø6		**Frailty status at follow-up**		
	All ($n=4350$)	**Robust ($n=3126$)**	**Pre-frail ($n=1224$)**	***P*[a]**
Women (%)	51.5	50.3	54.5	0.01
Age (years), mean (SD)	65.1 (5.7)	64.5 (5.5)	66.3 (6.1)	< 0.001
BMI (kg/m^2), mean (SD)	27.2 (4.1)	26.9 (3.8)	28.1 (4.6)	< 0.001
Cohabitant (%)	76.6	77.7	73.6	0.004
Good social support[b] (%)	90.0	91.3	86.5	< 0.001
Good self-rated health (%)	66.4	71.7	52.9	< 0.001
Daily smoking (%)				
Never	35.1	36.6	31.7	< 0.001
Previously	50.1	50.4	49.4	
Currently	14.7	13.1	18.9	
Education[c] (%)				
Lower secondary	33.2	30.5	40.1	< 0.001
Upper secondary	32.4	51.2	48.8	
Higher education	32.5	18.3	11.1	
Sedentary lifestyle (%)	16.1	10.4	31.0	< 0.001
High alcohol intake[d] (%)	6.4	6.9	5.0	< 0.001
Comorbidity[e] (%)	4.8	3.7	7.5	< 0.001
MMSE score, mean (SD)	28.3 (1.4)	28.3 (1.4)	28.1 (1.4)	0.02
Cod liver/fish oil supplements (%)	75.9	77.0	73.2	0.008
Frequency of fish intake				
Lean fish (%)				
0–3/month	17.1	16.4	18.8	0.1
1–3/week	67.2	67.5	66.6	
≥ 4/week	15.7	16.2	14.6	
Fatty fish (%)				
0–3/month	48.2	46.2	53.6	< 0.001
1–3/week	43.6	45.2	39.6	
≥ 4/week	8.1	8.7	6.8	
Total fish[f] (%)				
0–3/month	11.1	10.1	13.6	< 0.001
1–3/week	37.3	36.3	39.8	
≥ 4/week	51.7	53.6	46.6	

BMI, body mass index; MMSE, Mini-Mental State Examination; SD, standard deviation. *N* deviates slightly owing to missing data in specific covariates

[a] P-value: Student's t-test for continuous variables, chi-square test for categorical variables between robust and pre-frail groups

[b] Self-reported satisfactory level of good friends

[c] Primary/secondary school, modern secondary school; technical school, vocational school, 1–2 years senior high school or high school diploma; college/university

[d] Daily alcohol intake ≥10 g (women) or ≥20 g (men)

[e] The presence of ≥2 of the following diseases: cardiovascular disease (angina, heart attack, stroke), pulmonary disease (chronic bronchitis, asthma), diabetes and cancer

[f] The sum of fatty and lean fish intake

highlight the possible impact of dietary supplement use, model 3 was further adjusted for use of cod liver oil and long-chain omega-3 fatty acids (LCn-3FA) supplements.

Second, to elucidate the influence of long-term habitual fish intake, the models were run on the association between different patterns of stability of total fish intake over 21 years (Tromsø4, Tromsø6 and at follow-up) and pre-frailty at follow-up (Table 4). Participants included in the tracking analysis had data on lean and fatty fish intake from all three surveys. A stable low fish intake was chosen as the reference category.

Table 2 Frequency of fish intake and patterns of total fish intake for tracking sample ($n=3229$)[a]

Frequency of fish intake	Study waves of the Tromsø Study			
	Tromsø4 (1994-1995)	Tromsø6 (2007-08)	Tromsø7 (2015-16)	
Lean fish (%)				
0–3/month	12.5	16.8	11.6	
1–3/week	84.9	67.9	74.5	
≥4/week	2.5	15.3	13.8	
Fatty fish (%)				
0–3/month	55.4	47.9	44.6	
1–3/week	44.3	44.4	50.0	
≥4/week	0.3	7.7	5.5	
Total fish[a] (%)				
0–3/month	10.0	10.7	7.3	
1–3/week	65.9	37.0	35.2	
≥4/week	24.0	52.4	57.5	
Patterns of fish intake across Tromsø4, Tromsø6, Tromsø7				
	All ($n=3229$)	Robust ($n=2351$)	Pre-frail ($n=878$)	***P*[b]**
Stable patterns[c]				<0.001
Low	4.5	3.7	6.6	
Medium	42.3	41.9	43.4	
High	42.3	44.1	37.7	
Inconsistent[d]	10.9	10.4	12.3	

[a] The sum of fatty and lean fish intake

[b] *P* value: chi-square test

[c] Stable patterns of fish intake defined as the same reported frequency of intake in all three surveys, or two similar frequencies of intake plus one frequency of intake differing by one level

[d] Inconsistent patterns defined as patterns of fish intake that spread across the three levels of frequency of intake

To account for potential influence of already present frailty in the study sample, we repeated the main analysis as a sensitivity analysis in a sample where participants with frailty in Tromsø6 were excluded (Table S4). Further, supplementary analyses were performed to address bias from selective attrition of participants after Tromsø6. First, we compared characteristics of non-attenders after Tromsø6 versus participants who attended follow-up (Table S5). Second, inverse probability of participation weighting (IPPW) [47, 48] was applied to repeat the main analyses in a hypothetical study sample with 100% re-attendance at follow-up (Table S6). This pseudo-population was created through up-weighting characteristics likely to be lost with attrition. Specifically, follow-up participants were weighted by the inverse of their probability of participating at follow-up, to account for the absent weights of the non-attenders. Weights were based on the predicted likelihood of follow-up participation, predicted by the adjustment variables included in model 2, following Metten et al. [47]. Furthermore, we compared the characteristics of participants with complete versus incomplete data on fish intake in the three surveys (Table S7). As a sensitivity analysis to account for missing data, we repeated the tracking analysis in a sample with multiple imputed (MI) data on fish intake in the three surveys (Table S8). Fifty duplicate datasets were created via the predictive mean matching imputation method and estimates were combined with Rubin's rule [49].

Adjustment variables included in the statistical models were initially chosen from univariate analyses ($P<0.2$), in addition to clinical importance and considerations about confounding (as was the case for sex and dietary supplements). Subsequently, the multivariable models were built through careful evaluation of the contribution of each variable and comparisons between unrestricted and restricted versions of the model until it had an optimal fit [50]. Age and BMI were included as continuous variables whereas all others were categorical. Owing to the identification of non-linearity, BMI was included in both its linear and its squared form. There were no indications of multicollinearity between the adjustment variables and no statistically significant, clinically plausible interactions. All analyses were performed in STATA/MP 16. *P* values < 0.05 were considered to be statistically significant.

Table 3 Odds ratios (ORs) and 95% confidence intervals (CIs) for baseline fish intake and 8-year follow-up pre-frailty ($n=4350$)[a]

Dietary exposure (Tromsø6)	Model 1		Model 2		Model 3		P_{trend}[b]
	OR	95% CI	OR	95% CI	OR	95% CI	
Frequency of fish intake							
Lean fish	($n=4270$)		($n=3037$)		($n=3037$)		
0–3/month	Ref		Ref		Ref		< 0.001
1–3/week	0.82	0.69, 0.98	0.82	0.66, 1.03	0.82	0.66, 1.03	
≥ 4/week	0.69	0.55, 0.88	0.72	0.53, 0.97	0.72	0.53, 0.97	
Fatty fish	($n=4275$)		($n=3043$)		($n=3043$)		
0–3/month	Ref		Ref		Ref		0.04
1–3/week	0.75	0.65, 0.87	0.81	0.68, 0.97	0.81	0.68, 0.97	
≥ 4/week	0.65	0.49, 0.85	0.63	0.44, 0.92	0.63	0.44, 0.92	
Total fish[c]	($n=4195$)		($n=3000$)		($n=3000$)		
0–3/month	Ref		Ref		Ref		< 0.001
1–3/week	0.78	0.62, 0.97	0.87	0.66, 1.15	0.87	0.66, 1.16	
≥ 4/week	0.60	0.48, 0.75	0.68	0.52, 0.90	0.69	0.52, 0.91	

[a] Main analytic sample. *N* deviates owing to missing data in specific adjustment variables

[b] *P* value: Cochran-Armitage test for trend across groups

[c] The sum of fatty and lean fish intake

Model 1: adjusted for Tromsø6 age and sex. Model 2: additionally adjusted for Tromsø6 body mass index, education, comorbidity, smoking, activity level and self-reported health. Model 3: additionally adjusted for Tromsø6 cod liver oil and/or long-chain omega-3-fatty acids supplement use

Table 4 Odds ratios (ORs) and 95% confidence intervals (CIs) for patterns of fish intake and pre-frailty ($n=3229$)[a]

Patterns of total fish intake across Tromsø4, Tromsø6, Tromsø7	Model 1 ($n=3229$)		Model 2 ($n=2329$)		Model 3 ($n=2329$)	
	OR	95% CI	OR	95% CI	OR	95% CI
Stable patterns[b]						
Low[c]	Ref		Ref		Ref	
Medium	0.52	0.36, 0.75	0.69	0.44, 1.07	0.69	0.44, 1.07
High	0.41	0.28, 0.59	0.59	0.38, 0.92	0.59	0.38, 0.91
Inconsistent pattern[d]	0.61	0.40, 0.91	0.95	0.57, 1.56	0.94	0.57, 1.56

[a] Tracking sample: complete cases. Participants with available data on all questions on frequency of lean and fatty fish intake in Tromsø4, -6 and -7. *N* deviates owing to missing data in specific adjustment variables

[b] Stable patterns of fish intake defined as the same reported frequency of intake in all three surveys, or two similar frequencies of intake plus one frequency of intake differing by one leve

[c] Reference category

[d] Inconsistent patterns defined as patterns of fish intake that spread across the three levels of frequency of intake

Model 1: adjusted for Tromsø6 age and sex. Model 2: additionally adjusted for Tromsø6 body mass index, education, comorbidity, smoking, activity level and self-reported health. Model 3: additionally adjusted for Tromsø6 cod liver oil and/or long-chain omega-3-fatty acid supplement use

Results

Participants' characteristics and fish intake

In total, 28% ($n=1124$) of the main study population were classified as pre-frail at follow-up (Table 1). Of these, 84% ($n=1031$) presented with only one frailty characteristic (Table S9). The most prominent characteristic of physical frailty at follow-up was by far self-reported low physical activity level, which was the only frailty characteristic present in 51% of the pre-frail participants (Table S9). About one third of the participants had missing frailty data, and 23% had missing data on two characteristics. The prevalence of pre-frailty increased with age (Table S10).

In Tromsø6, the mean age was 65 years (range 57–87 years) and 52% were women (Table 1). Pre-frail participants differed from robust participants as they were more likely to be women, older, daily smokers, inactive, lower educated and have higher BMI than robust participants. They were also less likely to be satisfied with self-perceived support from friends and their own health.

More pre-frail participants than robust participants lived alone, and the proportion of pre-frail participants with comorbidity was twice as high as among robust participants (Table 1). Three-quarters of all participants used cod liver oil and/or LCn-3FA supplements, more commonly used by robust than by pre-frail participants.

Comparing non-attenders after Tromsø6 (36%) versus participants who re-attended Tromsø7 showed that the latter had notably more favourable health and socioeconomic characteristics but that fish intakes were similar (Table S5).

For the tracking subsample, differences were similar between pre-frail and robust participants as in the main sample (Table S3). Comparing participants with complete versus incomplete data on fish intake in the three surveys showed that complete cases had a slightly more favourable health and socioeconomic profile (Table S7).

In Tromsø6, the main sample ate lean fish more frequently than fatty fish (Table 1). Robust participants ate fatty and total (but not lean) fish more frequently than pre-frail participants. Of the robust participants, 54% had a medium or high intake (≥ 1/week) of fatty fish compared with 46% of pre-frail participants ($P < 0.001$). For total fish, 90% of robust and 86% of pre-frail participants had a medium or high intake ($P < 0.001$).

Also for the tracking sample, lean fish was eaten more frequently than fatty fish at all times (Table 2). The frequency of intake of fatty and total fish appeared to increase between surveys. For fish intake over 21 years, the vast majority had either a stable medium (42%) or stable high (42%) pattern of fish intake (Table 2). A stable low pattern of fish intake was slightly more common among pre-frail than robust participants (7% vs 4%), while a stable high pattern over time was more common among robust than pre-frail participants (44% vs 38%) ($P < 0.001$).

Fish intake in Tromsø6 and pre-frailty 8 years later

Overall, the main analysis showed that a more frequent fish intake in Tromsø6 was associated with lower odds of pre-frailty 8 years later (P value for trend < 0.05) (Table 3). The observed associations from the multivariable model (model 2) and after further adjustment for dietary supplement use (model 3) were similar.

Fully adjusted analysis (model 3) showed that a high intake (≥ 4/week) of lean fish was associated with 28% (OR = 0.72, 95% CI = 0.53, 0.97) lower odds of pre-frailty at follow-up 8 years later compared with a low intake (0–3/month). For fatty fish, a medium (1–3/week) or high intake in Tromsø6 was associated with 19% (OR = 0.81, 95% CI = 0.68, 0.97) and 37% (OR = 0.63, 95% CI = 0.44, 0.92) lower odds of pre-frailty after 8 years, respectively, compared with a low intake. Fully adjusted analysis of total fish intake showed that the odds of pre-frailty after 8 years was 31% lower for participants with a high compared with a low frequency of intake (OR = 0.69, 95% CI = 0.52, 0.91). Results were similar, albeit slightly amplified, in sensitivity analysis excluding pre-frail and frail individual at baseline (Table S4). Fully adjusted sensitivity analyses with IPPW showed no significant association between frequency of fish intake in Tromsø6 and pre-frailty 8 years later (Table S6).

Patterns of fish intake over 21 years and pre-frailty

Fully adjusted tracking analysis showed that a stable high frequency of intake across Tromsø4, Tromsø6 and Tromsø7 was associated with 41% lower odds of pre-frailty (OR = 0.59, 95% CI = 0.38, 0.91) in Tromsø7, compared with a stable low pattern (Table 4). Results were similar with MI (56% missing data on fish intake) (Table S8).

Discussion

In the present prospective cohort study, we found that a higher frequency of (lean, fatty and total) fish intake was significantly associated with lower odds of physical pre-frailty after 8 years in older community-dwelling adults in Norway. Moreover, a pattern of consistent high frequency of total fish intake over 21 years was associated with lower odds of pre-frailty.

Overall, the main study population was a relatively healthy sample of older residents in Tromsø, Northern Norway. Considering that individuals with low cognitive skills in Tromsø6 were excluded, alongside the need for physical attendance in the Tromsø study, we assume that the study population is mainly community-dwelling.

The observed prevalence of pre-frailty in the present study was lower than reported among community-dwelling older adults worldwide [51], in Europe [52], and Tromsø5 study participants aged ≥ 70 years in 2001 [53]. These discrepancies may be partly explained by the use of different modifications of Fried's frailty definition [54]. Moreover, another study from the Tromsø Study has shown increased grip strength in more recent birth cohorts of older participants [55]. Considering that there were 15 years between the measures of frailty status, this may partly explain the differences in frailty prevalence reported in the present study versus the study by Langholz et al. [53]. In line with previous research, the prevalence of pre-frailty in Tromsø7 was higher in women and increased with age [5, 51–53].

The overall relatively high frequency of fish intake observed in all three surveys was somewhat expected, considering that older Norwegians have been found to eat more fish than younger generations and that fish

intake, in general, is high in Northern Norway [27–30]. The observed higher frequency of fish intake in the robust compared with the pre-frail participants, taken together with their better health and socioeconomic characteristics, is supported by a recent, large systematic review that found that seafood consumers were more likely to be older, more affluent, educated and physically active and less likely to be smokers compared with non-seafood consumers [56]. In contrast to this, the frequency of fish intake was similar for dropouts after Tromsø6 compared with those re-attending Tromsø7, even though the sociodemographic characteristics in the latter group were slightly more favourable.

Longitudinal associations between frequency of fish intake and pre-frailty

Our findings suggest that how often one eats fish in late adulthood may influence later odds of pre-frailty. This emphasizes the importance for this age group of adhering to the Norwegian Dietary Guidelines' recommendations of eating fish two to three times a week [20]. A benefit and risk assessment of fish in the Norwegian diet recently concluded that there were positive health benefits associated with increasing the Norwegian adult's fish intake to the upper end of the recommended intake range [57]. Although not directly comparable, our results agree with this. The strengths of the observed associations between frequency of fish intake and pre-frailty increased with higher frequency of intake.

As the existing literature on fish intake and pre-frailty is particularly scarce, the comparison of our results is limited to studies focusing on frailty or frailty-related outcomes.

The observed beneficial association between increased frequency of fatty fish intake and later pre-frailty is supported by findings from a longitudinal Spanish study in 1592 community-dwelling adults aged ≥60 years conducted by García-Esquinas et al. [21]. They observed an inverse association between increased daily estimated intake of fatty fish and accumulation of age-related health deficits 6 years later. The health deficit accumulation index is another widespread and more comprehensive measure of frailty than Fried's physical phenotype [58]. In addition, a cross-sectional study conducted in rural coastal Ecuador showed a stepwise decrease in frailty scores for each additional weekly serving of fatty fish consumed among community dwellers aged 60–69 years [23]. Notably, there was no association between fish intake and frailty status in the participants aged ≥70 years, for whom the authors speculated that the effects of age superseded the positive effects of fatty fish.

For lean fish, the observed beneficial association between high intakes and pre-frailty is in accordance with a Saudi Arabian intervention study which showed that eating lean fish for lunch twice a week for 10 weeks significantly increased muscle mass and walking speed in 22 adults (≥50 years) [26]. However, in the longitudinal study by García-Esquinas et al., they did not find any association between intake of lean fish and healthy ageing [21].

In line with our findings, García-Esquinas et al. did, however, observe reduced deficit accumulation scores with increasing quintiles of total fish intake [21]. Furthermore, an Irish cross-sectional study in community-dwelling older adults (≥65 years) observed significantly higher odds of Fried's physical frailty among those in the lowest tertile of intake of fish and fish products compared with the highest [22]. In addition, a cross-sectional study in Japanese female outpatients with rheumatoid arthritis found that, of 20 foods assessed, fish intake more than twice a week was identified as independently negatively associated with pre-frailty/frailty (pre-frail and frailty combined as outcome) [24].

Taken together, the comparability of the results from these studies with our study is somewhat limited. The levels of fish intake differs, and all, except the study by O'Connell et al. [22], use different frailty definitions, have no mention of dietary supplements, and include study populations and settings that differ greatly from the relatively healthy community-dwelling older adults from Northern Norway [21–24, 26].

Our results from the tracking analysis showing lower odds of pre-frailty from a consistent high frequency of intake compared with consistent low frequency of intake was as hypothesized. To the best of our knowledge, no earlier study has tracked fish intake over time in relation to frailty or other age-related health outcomes.

Some of the plausible biological pathways between nutrients in fish and health that could be relevant in the observed association between fish intake and pre-frailty include vitamin D's beneficial effect on bone health and muscle function [14, 19, 59]; the anti-inflammatory properties of LCn-3FA [14, 59, 60], or lower rate of muscle loss from increased intake of high-quality fish protein [14, 59, 61]. However, it is important to emphasize that owing to the nature of the frequency data and the long follow-up times, what we have truly assessed is the *habit* of eating fish and not the biological properties of the fish and its nutrients. Moreover, one could speculate that the observed protective effect of frequent fish intake, in participants where fish makes up a large proportion of their total diet, simply reflects a subsequent lower intake of other and perhaps less healthy foods.

Strengths and limitations

A limitation of the study is the self-reported data, which introduces risk of information bias. Unfortunately, self-reported dietary data are typically misreported, either consciously or unconsciously [62]. Given the general status of fish as a healthy food [63], one could speculate that fish intakes are over-reported. Another limitation is that the two variables on fish intake that provided the basis for the analyses were too crude to capture the participant's absolute intake. Moreover, the variables depend on the participants' prior knowledge on what constitutes fatty and lean fish and this may have introduced uncertainty to the study. Additional information about intake of other fish products and fish spread was available in the different surveys, albeit at different levels, and, therefore, to facilitate comparability between time points, the focus was kept on the two variables lean and fatty fish.

Another limitation is the variation within the stable patterns of fish intake, owing to the definition criteria which allows for one differing frequency of intake. Thus, patterns might vary substantially within categories, depending on whether the 'one off' is a higher or lower frequency than the other two, or in what survey the different frequency of intake was reported.

Selection bias is a common limitation in cohort studies, because participants tend to be healthier and have better socioeconomic status than non-attenders [64]. This is emphasized by the overall good health of the study population and the low prevalence of pre-frailty in Tromsø7. In addition, the predominance of pre-frail participants with a frailty score of only 1, where many had low physical activity level as their only frailty characteristic may reflect that the pre-frail group largely consisted of sedentary, but otherwise healthy, individuals. The slightly weaker association observed between frequency of fish intake and pre-frailty in the IPPW sensitivity analysis could be explained by a lower degree of selection bias. Considering the observed differences between those who participated in Tromsø7 versus the non-attenders, the pseudo-population included in the IPPW analysis, with 100% participation in Tromsø7, was older and more heterogeneous than the main study population. Thus, the effects of age and poorer health might to some extent have superseded the positive effects of frequent fish intake on later pre-frailty in these participants. Notably, the substantial level of missing frailty data might have contributed to an incorrectly measured prevalence of pre-frailty and biased results.

With these limitations in mind, the study's results should be interpreted somewhat cautiously and their generalization is limited to relatively healthy, community-dwelling, older Norwegian adults. However, in favour of our findings of an inverse association between increased frequency of fish intake and pre-frailty after 8 years, were the results from the sensitivity analysis performed after exclusion of baseline pre-frail/frail participants and the tracking analysis with MI.

The strengths of the study include its longitudinal study design, the large study sample, and the use of validated instruments for frailty assessment. In addition, the available data were scrutinized to thoroughly assess the fish–pre-frailty association by investigating lean, fatty, and total fish, the impact of different lengths of follow-up and the specific adjustment for use of cod liver oil and LCn-3FA supplements. Furthermore, the performance of supplementary analyses to account for inherent and unavoidable weaknesses of observational studies, like the already mentioned risk of attrition and the influence of missing data, adds transparency and value to the interpretation of the results.

Conclusions

This study shows that higher frequency of fish intake among middle-aged and older community-dwelling adults reduce later odds of pre-frailty. Thus, our study emphasizes the importance of a frequent fish intake to prevent pre-frailty and facilitate healthy ageing.

Abbreviations

BMI	Body mass index
CI	Confidence interval
IPPW	Inverse participation probability weighting
LCn-3FA	Long-chain omega-3 fatty acids
MI	Multiple imputation
MMSE	Mini-Mental State Examination
OR	Odds ratio

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12877-023-04081-z.

Additional file 1: Table S1. Original and modified categories of frequency of fish intake in the Tromsø Study. **Table S2.** Modifications of the frailtyphenotype in the Tromsø7 Study (2015–2016). **Table S3.** Characteristics of tracking sample in Tromsø4 and Tromsø6 (*n*=3229). **Table S4.** Odds ratios (ORs) and 95% confidence intervals (CIs) for fish intake and 8-year follow-up pre-frailty after exclusion of baseline frailty ($n = 3219$)[a]. **Table S5.** Characteristics of participants in Tromsø6 by Tromsø7 participation status ($n = 6837$)[a]. **Table S6.** Odds ratios (ORs) and 95% confidence intervals (CIs) for baseline fish intake and pre-frailty with inverse probability weights[a] ($n = 6183$)[b]. **Table S7.** Characteristics of participants in Tromsø6 with complete and incomplete data on fish intake ($n = 5750$)[a]. **Table S8.** Odds ratios (ORs) and 95% confidence intervals (CIs) for patterns of fish intake and pre-frailty using multiple imputation (MI)[a] ($n = 5750$)[b]. **Table S9.** Onset of physical frailty characteristics in Tromsø7 ($n = 4350$)[a]. **Table S10.** Frailty prevalence in Tromsø7 stratified by age ($n = 4350$)[a].

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Authors' contributions
All authors were involved in the study conception and design. MHC supervised the project. DMK analysed the data. DMK, MHC and LFA drafted the original manuscript. BHS, MT and AH contributed with statistical guidance. All authors interpreted the results and contributed to the discussion, revision and editing of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The legal restriction on data availability is set by the Tromsø Study Data and Publication Committee in order to control for data sharing, including publication of datasets with the potential of reverse identification of de-identified sensitive participant information. The data that support the findings of this study are available from the Tromsø Study but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the Tromsø Study Data and Publication Committee. Contact information: The Tromsø Study, Department of Community Medicine, Faculty of Health Sciences, UiT The Arctic University of Norway; e-mail: tromsous@uit.no. A detailed overview of the data collection process and links to the main questionnaires, can be found on the Tromsø Study's website (https://uit.no/research/tromsostudy). All variables collected in the Tromsø Study can be found in NESSTAR (http://tromsoundersokelsen.uit.no/tromso/).

Declarations

Ethics approval and consent to participate
Informed consent was obtained from all participants for being included in the study. The study was conducted in accordance with the Declaration of Helsinki. The project was approved by Regional Committees for Medical and Health Research Ethics (REK; 2019/43798).

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no conflict of interests.

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Publisher's Note

Supplementary files

Additional file 1: Table S1–S10

Table S1 Original and modified categories of frequency of fish intake in the Tromsø Study

Frequency of fish intake	Study waves of the Tromsø Study					
	Tromsø4 (1994–1995)[a]		**Tromsø6 (2007–2008)**		**Tromsø7 (2015–2016)**	
Lean fish	**How many times per week do you usually eat lean fish (e.g. cod) for dinner?**		**How often do you usually eat lean fish?**		**How often do you usually eat lean fish (cod, saithe)?**	
	Original	*Modified*	*Original*	*Modified*	*Original*	*Modified*
Low	Never <1	0–3 times a month	0–1 times a month 2–3 times a month	0–3 times a month	0–1 times a month 2–3 times a month	0–3 times a month
Medium	1 2–3	1–3 times a week	1–3 times a week	1–3 times a week	1–3 times a week	1–3 times a week
High	4–5 Approx. daily	≥4 times a week	4–6 times a week 1–2 times a day	≥4 times a week	4–6 times a week ≥1 time a day	≥4 times a week
Fatty fish	**How many times per week do you usually eat fatty fish (e.g. salmon/redfish) for dinner?**		**How often do you usually eat fatty fish (e.g. salmon, trout, mackerel, herring, halibut, redfish)?**		**How often do you usually eat fatty fish (salmon, trout, redfish, mackerel, herring, halibut)?**	
	Original	*Modified*	*Original*	*Modified*	*Original*	*Modified*
Low	Never <1	0–3 times a month	0–2 times a month 2–3 times a month	0–3 times a month	0–2 times a month 2–3 times a month	0–3 times a month
Medium	1 2–3	1–3 times a week	1–3 times a week	1–3 times a week	1–3 times a week	1–3 times a week
High	4–5 Approx. daily	≥4 times a week	4–6 times a week 1–2 times a day	≥4 times a week	4–6 times a week ≥1 time a day	≥4 times a week

Approx.: approximately. [a]Information collected only among participants in Tromsø4 aged <70 years. Participants aged ≥70 years (n = 15) were given a different questionnaire with other, and incomparable, frequency intervals of fatty and lean fish intake.

Table S2 Modifications of the frailty phenotype in the Tromsø7 Study (2015–2016)

	Criteria for frailty by Fried et al. 2001	**Criteria for frailty in Tromsø7**
Weight loss	Self-reported, from the question 'In the last year, have you lost more than 10 pounds unintentionally (i.e. not due to dieting or exercise)?'. If yes, then frail for weight loss criterion. Or, at follow-up: ≥5% unintentional loss of body weight in prior year (by direct measurement of weight at follow-up)	Self-reported, based on a question from the Malnutrition Universal Screening Tool: 'Have you involuntarily lost weight during the last 6 months?'. If yes, then frail for the weight loss criterion
Exhaustion	Self-reported, based on two questions from the Center for Epidemiologic Studies Depression Scale: (a) I felt that everything I did was an effort (b) I could not get going. 'How often in the last week did you feel this way?' 0 = rarely or none of the time (<1 day) 1 = some or a little of the time (1–2 days) 2 = a moderate amount of the time (3–4 days) 3 = most of the time Answer 2 or 3 to either of these questions led to categorisation as frail for the exhaustion criterion	Self-reported, based on the Hopkins Symptoms Checklist 10: 'Have you experienced any of this the last week: That everything is a struggle?' 1 = No complaint 2 = Little complaint 3 = Pretty much 4 = Very much Answer 3 or 4 led to categorisation as frail by the exhaustion criterion
Physical activity	Self-reported, based on the Minnesota Leisure Time Activity short questionnaire asking about walking, chores (moderately strenuous), mowing the lawn, raking, gardening, hiking, jogging, biking, exercise cycling, dancing, aerobics, bowling, golf, singles tennis, doubles tennis, racquetball, calisthenics, swimming. Kilocalories per week expended were calculated using standardised algorithm. The lowest 20% was identified for each sex *Frailty cut-off for physical activity:* *Men*: <383 kcal of physical activity per week *Women*: <270 kcal of physical activity per week	Self-reported, based on Saltin–Grimby Physical Activity Level Scale. Describe your exercise and physical exertion in leisure time over the last year: 1 = Reading, watching TV/screen or other sedentary activity? 2 = Walking, cycling or other forms of exercise at least 4 hours a week? 3 = Participation in recreational sports, heavy gardening, snow shovelling etc. at least 4 hours a week? 4 = Participation in hard training or sports competitions, regularly several times a week

			Answer 1 led to categorisation as frail for the physical activity criterion	
Walking speed	Time to Walk test: walk 15 feet at usual pace (s). Stratified by sex and height (gender-specific cut-off at medium height). Lowest 20% were identified, resulting in the following cut-off for the walking speed criterion of frailty:		Short Physical Performance Battery walking test: fastest (s) of two times to walk 4 m on average pace. Stratified by sex and height. Calculated from s/4 m to s/15 feet (4.572 m)for adaption to Fried's criteria: (s/4 m) × 1.143 = s/4.572 m	
	Men	*Cut-off (s)*	*Men*	*Cut-off (s)*
	Height ≤173 cm	≥7	Height ≤173 cm	≥7
	Height >173 cm	≥6	Height >173 cm	≥6
	Women	*Cut-off (s)*	*Women*	*Cut-off (s)*
	Height ≤159 cm	≥7	Height ≤159 cm	≥7
	Height >159 cm	≥6	Height >159 cm	≥6
Grip strength	Measured by Jamar dynamometer (kg), maximal strength of three trials in dominant hand. Stratified by sex and BMI quartiles. Lowest 20% were identified, resulting in the following cut-off for frailty:		Measured by Jamar dynamometer (kg), maximal of three trials in each hand (six measurements). Stratified by sex and BMI quartiles:	
	Men	*Cut-off (kg)*	*Men*	*Cut-off (kg)*
	BMI ≤24	≤29	BMI ≤24	≤29
	BMI 24.1–26	≤30	BMI 24.1–26	≤30
	BMI 26.1–28	≤30	BMI 26.1–28	≤30
	BMI >28	≤32	BMI >28	≤32
	Women	*Cut-off (kg)*	*Women*	*Cut-off (kg)*
	BMI ≤23	≤17	BMI ≤23	≤17
	BMI 23.1–26	≤17.3	BMI 23.1–26	≤17.3
	BMI 26.1–29	≤18	BMI 26.1–29	≤18
	BMI >29	≤21	BMI >29	≤21
Frailty score	0 = Not frail/robust 1–2 = Intermediate/pre-frail ≥3 = Frail		0 = Not frail/robust 1–2 = Intermediate/pre-frail ≥3 = Frail	

Table S3 Characteristics of tracking sample in Tromsø4 and Tromsø6 (n=3229)

Characteristics	**Study waves of the Tromsø Study**							
	Tromsø4				**Tromsø6**			
	All (*n* = 3229)	**Robust (*n* = 2351)**	**Pre-frail (*n* = 878)**	***P*[a]**	**All (*n* = 3229)**	**Robust (*n* = 2351)**	**Pre-frail (*n* = 878)**	***P*[a]**
Women (%)	50.1	49.0	53.1	0.04	50.1	49.0	53.1	0.04
Age (years), mean (SD)	51.9 (5.4)	51.5 (5.2)	53.1 (5.7)	<0.001	64.9 (5.4)	64.5 (5.2)	66.1 (5.7)	<0.001
BMI (kg/m^2), mean (SD)	25.7 (3.5)	25.4 (3.3)	26.4 (3.8)	<0.001	27.2 (4.0)	26.8 (3.7)	28.2 (4.6)	<0.001
Cohabitant (%)	85.4	85.9	84.2	0.2	79.0	79.9	76.8	0.05
Good social support[b] (%)	82.3	83.0	80.1	0.06	90.5	91.6	87.5	0.001
Good self-rated health (%)	71.7	75.2	62.3	<0.001	66.5	71.5	53.4	<0.001
Daily smoking (%)								
Never	34.6	36.6	29.2		35.1	36.8	30.5	
Previously	37.1	37.1	37.2	<0.001	52.4	51.1	52.1	<0.001
Currently	28.3	26.3	33.6		13.6	12.1	17.3	
Education[c] (%)								
Lower secondary	32.3	30.3	37.6		31.0	28.9	36.5	
Upper secondary	36.1	35.9	36.4	<0.001	35.7	35.3	36.9	<0.001
Higher education	31.7	33.8	26.0		33.3	35.9	26.6	
Sedentary lifestyle (%)	32.5	29.2	41.4	<0.001	15.0	9.9	29.1	<0.001
High alcohol intake[d] (%)	1.9	2.0	1.8	0.7	6.9	7.3	5.9	0.15
Comorbidity[e] (%)	0.9	0.9	0.9	0.9	4.7	3.4	8.2	<0.001
MMSE score					28.3 (1.4)	28.3 (1.4)	28.1 (1.4)	0.008
Cod liver/fish oil supplements (%)	48.2	49.2	45.6	0.1	76.3	77.5	72.9	0.006

BMI, body mass index; MMSE, Mini-Mental State Examination; SD, standard deviation. *N* deviates slightly owing to missing data in specific covariates. [a]P-value: Student's t-test for continuous variables, chi-square test for categorical variables between robust and pre-frail groups. [b]Self-reported satisfactory level of good friends. [c]Primary/secondary school, modern secondary school; technical school, vocational school, 1-2 years senior high school or high school diploma; college/university. [d]Daily alcohol intake ≥10 g (women) or ≥20 g (men). [e]The presence of ≥2 of the following diseases: cardiovascular disease (angina, heart attack, stroke), pulmonary disease (chronic bronchitis, asthma), diabetes and cancer.

Table S4 Odds ratios (ORs) and 95% confidence intervals (CIs) for fish intake and 8-year follow-up pre-frailty after exclusion of baseline frailty (n = 3219)[a]

Dietary exposure (Tromsø6)	Model 1		Model 2		Model 3		P_{trend}[b]
	OR	95% CI	OR	95% CI	OR	95% CI	
Frequency of fish intake							
Lean fish		(n = 3158)		(n = 2379)		(n = 2379)	
0–3/month	Ref.		Ref.		Ref.		
1–3/week	0.87	0.69, 1.10	0.74	0,57, 0.98	0.74	0.56, 0.98	0.3
≥4/week	0.73	0.54, 1.00	0.62	0.43, 0.89	0.61	0.43, 0.89	
Fatty fish		(n = 3172)		(n = 2399)		(n = 2399)	
0–3/month	Ref.		Ref.		Ref.		
1–3/week	0.74	0.62, 0.89	0.71	0.57, 0.87	0.71	0.57, 0.88	<0.001
≥4/week	0.59	0.41, 0.84	0.39	0.24, 0.64	0.40	0.24, 0.65	
Total fish[c]		(n = 3110)		(n = 2354)		(n = 2354)	
0–3/month	Ref.		Ref.		Ref.		
1–3/week	0.84	0.62, 1.12	0.75	0.53, 1.06	0.75	0.54, 1.06	<0.001
≥4/week	0.62	0.46, 0.82	0.52	0.37, 0.73	0.53	0.38, 0.74	

[a]Main analytic sample after exclusion of participants defined as frail or pre-frail in Tromsø6. *N* deviates owing to missing data in specific adjustment variables. [b]*P* value: Cochran-Armitage test for trend across groups. [c]The sum of fatty and lean fish intake. **Model 1:** adjusted for Tromsø6 age and sex. **Model 2:** additionally adjusted for Tromsø6 body mass index, education, comorbidity, smoking and self-reported health. **Model 3:** additionally adjusted for Tromsø6 cod liver oil and/or long-chain omega-3-fatty acids supplement use.

Table S5 Characteristics of participants in Tromsø6 by Tromsø7 participation status (n = 6837)[a]

Tromsø6 characteristics	Did not attend Tromsø7 (n = 2428)	Attended Tromsø7 (n = 4409)	P^b
Women (%)	52.4	51.7	6
Age (years), mean (SD)	70.1 (8.0)	65.1 (5.7)	<0.001
BMI (kg/m^2), mean (SD)	27.0 (4.4)	27.2 (4.1)	0.05
Cohabitation (%)	65.1	76.4	<0.001
Good self-rated health (%)	49.3	66.0	<0.001
Daily smoking (%)	22.0	14.8	<0.001
Education[c] (%)			
Lower secondary	46.2	33.4	<0.001
Upper secondary	30.3	34.3	
Higher education	23.5	32.3	
Sedentary lifestyle (%)	29.2	16.4	<0.001
High alcohol intake[d] (%)	4.9	6.3	0.02
Comorbidity[e] (%)	12.8	4.9	<0.001
MMSE score, mean (SD)	28.0 (1.5)	28.3 (1.4)	<0.001
Cod liver/fish oil supplement use (%)	74.8	76.1	0.2
Fish intake			
Lean fish			
0–3/month	20.8	17.2	<0.001
1–3/week	62.0	67.1	
≥4/week	17.2	15.7	
Fatty fish			
0–3/month	49.5	48.3	0.03
1–3/week	40.8	43.5	
≥4/week	9.7	8.2	
Total fish[f]			
0–3/month	14.4	11.2	0.001
1–3/week	35.2	37.2	
≥4/week	50.5	51.6	

BMI, body mass index; MMSE, Mini-Mental State Examination; SD, standard deviation. [a]Participants in Tromsø6 <57 years, MMSE score ≥24 with data on lean and/or fatty fish intake. *N* deviates slightly owing to missing data in specific covariates. [b]*P* value: Student's t-test for continuous variables, chi-square test for categorical variables. [c]Primary/secondary school, modern secondary school; technical school, vocational school, 1–2 years senior high school or high school diploma; college/university. [d]Daily alcohol intake ≥10 g (women) or ≥20 g (men). [e]The presence of two or more of the following diseases: cardiovascular disease (angina, heart attack, stroke), pulmonary disease (chronic bronchitis, asthma), diabetes and cancer. [f]The sum of fatty and lean fish intake.

Table S6 Odds ratios (ORs) and 95% confidence intervals (CIs) for baseline fish intake and pre-frailty with inverse probability weights[a] (n = 6183)[b]

Dietary exposure (Tromsø6)	Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI
Lean fish						
0–3/month	Ref.		Ref.		Ref.	
1–3/week	0.79	0.65, 0.96	0.84	0.66, 1.07	0.84	0.66, 1.07
≥4/week	0.69	0.53, 0.91	0.79	0.58, 1.09	0.79	0.57, 1.08
Fatty fish						
0–3/month	Ref.		Ref.		Ref.	
1–3/week	0.79	0.67, 0.92	0.82	0.68, 0.99	0.83	0.69, 1.00
≥4/week	0.72	0.53, 0.99	0.71	0.49, 1.04	0.71	0.49, 1.04
Total fish[c]						
0–3/month	Ref.		Ref.		Ref.	
1–3/week	0.79	0.61, 1.01	0.90	0.66, 1.22	0.90	0.66, 1.22
≥4/week	0.62	0.49, 0.79	0.75	0.55,1.01	0.75	0.55, 1.01

[a]Probability of re-attending Tromsø7 estimated based on Tromsø6 characteristics age, sex, body mass index, physical activity, comorbidity, education and self-reported health. Subsequently, inverse weights of the estimated probability of attendance were calculated and applied to the study population. This created a pseudopopulation with 100% re-attendance in which characteristics of non-attenders were up-weighted. [b]Hypothetical study population based on Tromsø6 participants (n = 6837). [c]The sum of fatty and lean fish intake. **Model 1:** adjusted for Tromsø6 age and sex. **Model 2:** additionally adjusted for Tromsø6 BMI, education, comorbidity, smoking, activity level and self-reported health. **Model 3:** additionally adjusted for Tromsø6 cod liver oil and/or long-chain omega-3-fatty acid supplement use.

Table S7 Characteristics of participants in Tromsø6 with complete and incomplete data on fish intake (n = 5750)[a]

Characteristics in Tromsø6	Incomplete data on fish intake (n = 2521)	Complete data on fish intake (n = 3229)	P[b]
Women (%)	52.8	50.1	0.10
Age (years), mean (SD)	62.9 (6.2)	5.4	<0.001
BMI (kg/m^2), mean (SD)	27.3 (4.2)	4.0	0.3
Cohabitant (%)	69.2	79.0	0.1
Good self-rated health (%)	65.3	66.5	0.7
Daily smoking (%)	18.7	13.6	<0.001
Education[c] (%)			
Lower secondary	58.2	31.2	
Upper secondary	21.5	35.6	<0.001
Higher education	20.3	33.2	
Sedentary lifestyle (%)	19.2	15.0	0.003
High alcohol intake[d] (%)	4.6	6.9	0.009
Comorbidity[e] (%)	4.8	4.7	0.9
MMSE score	28.3 (1.4)	28.3 (1.4)	0.8

BMI, body mass index; MMSE, Mini-Mental State Examination; SD, standard deviation. *N* deviates slightly owing to missing data in specific covariates. [a]Study sample resembles eligible participants in Tromsø6 (see Figure 1) except for that Tromsø7 attendance was not an exclusion criterion, and the exclusion criterion 'No data on fish intake in Tromsø6' was replaced by 'No data on fish intake in Tromsø4, Tromsø6 or Tromsø7' (i.e. not at all). Thus, participants are of eligible age and with data on minimum one fish variable from any of the three surveys. [b]*P* value: Student's *t*-test for continuous variables, chi-square test for categorical variables. [c]Primary/secondary school, modern secondary school; technical school, vocational school, 1–2 years senior high school or high school diploma; college/university. [d]Daily alcohol intake ≥10 g (women) or ≥20 g (men). [e]The presence of two or more of the following diseases: cardiovascular disease (angina, heart attack, stroke), pulmonary disease (chronic bronchitis, asthma), diabetes and cancer.

Table S8 Odds ratios (ORs) and 95% confidence intervals (CIs) for patterns of fish intake and pre-frailty using multiple imputation (MI)[a] (n = 5750)[b]

Patterns of total fish intake	**Model 1 (n = 5750)**		**Model 2 (n = 5750)**		**Model 3 (n = 5750)**	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Stable[c]						
Low[d]	Ref.		Ref.		Ref.	
Medium	0.64	0.48, 0.85	0.76	0.55, 1.03	0.76	0.55, 1.03
High	0.45	0.34, 0.60	0.57	0.42, 0.77	0.57	0.42, 0.78
Inconsistent[e]	0.66	0.47, 0.92	0.77	0.54, 1.12	0.78	0.54, 1.12

[a]Multiple imputation (MI) was performed to address missing data on frequency of intake of fatty and lean fish in Tromsø4, Tromsø6 and Tromsø7. These variables provided the basis for the exposure variable 'Patterns of total fish intake' in this analysis. Fifty duplicate datasets were created via predictive mean matching imputation method. The imputation model included the outcome (pre-frailty) and all descriptive variables collected in Tromsø6 (see Table 1). Estimates from the 50 imputed datasets were combined with Rubin's rules to obtain ORs and 95% CIs. [b]Study sample resembles eligible participants in Tromsø6 (see Figure 1) except for that Tromsø7 attendance was not an exclusion criterion, and the exclusion criterion 'No data on fish intake in Tromsø6' was replaced by 'No data on fish intake in Tromsø4, Tromsø6 or Tromsø7' (i.e. not at all). Thus, participants are of eligible age and with data on minimum one fish variable from any of the three surveys. [c]Stable patterns of fish intake defined as the same reported frequency of intake in all three surveys, or two similar frequencies of intake plus one frequency of intake differing by one level. [d]Reference category. [e]Inconsistent patterns defined as patterns of fish intake that spread across the three levels of frequency of intake. **Model 1:** adjusted for Tromsø6 age and sex. **Model 2:** adjusted for Tromsø6 age, sex, BMI, education, comorbidity, smoking, activity level and self-reported health. **Model 3:** additionally adjusted for Tromsø6 cod liver oil and/or long-chain omega-3-fatty acids supplement use.

Table S9 Onset of physical frailty characteristics in Tromsø7 (n = 4350)[a]

	All (n = 4350)	**Frailty score 1 (n = 1031)**	**Frailty score 1–2 (n = 1224)[b]**
Frequency of frailty components (%)[c]			
Exhaustion, n = 4139	2.9	7.8	10.5
Slow walking speed, n = 3182	5.4	13.7	19.3
Low grip strength, n = 3185	6.3	17.6	22.1
Weight loss, n = 4194	7.3	23.3	26.1
Low physical activity, n = 4012	15.5	51.4	54.3

[a]Main analytic sample. [b]Pre-frail participants. [c]Percentage prevalence calculated among participants with valid data on the specific frailty components (left column).

Table S10 Frailty prevalence in Tromsø7 stratified by age (n = 4350)[a]

	Robust (n = 3126)	**Pre-frail (n = 1224)**	P_{trend}[b]
Age (years) in Tromsø7			
65–69, n = 1373	76.3	23.7	
70–74, n = 1497	75.4	24.7	<0.001
75–79, n = 843	67.1	32.9	
≥80, n = 637	60.4	39.6	

[a]Main analytic sample. [b]P value: Cochran-Armitage test for trend across groups.

Paper III

III

Appendices

1. Links to invitation letters, consent forms and questionnaires in Tromsø4 to Tromsø7
2. Selected pages from questionnaires used in Tromsø4 (1994–95) with food-related questions
3. Selected pages from questionnaires used in Tromsø5 (2001) with food-related questions
4. Selected pages from questionnaires used in Tromsø6 (2007–08) with food-related questions
5. Selected pages from questionnaires used in Tromsø7 (2015–16) with food-related questions
6. Food frequency questionnaire in Tromsø7 (2015–16)
7. Study approval from the Regional Committees for Medical and Health Research Ethics (REK)

Appendix 1

Links to invitation letters, consent forms and questionnaires in Tromsø4 to Tromsø7

Tromsø4 (1994–5)

- Invitation: https://uit.no/Content/271754/T4_Invitation.pdf
- Consent form: https://uit.no/Content/710357/cache=20203011130444/samtykkerklaering.tromso4.pdf
- Questionnaire 1 (Q1): https://uit.no/Content/271764/T4_Q1.pdf
- Questionnaire 2 (Q2) <70 years: https://uit.no/Content/430574/T4_Q2_U70.pdf
- Q2 ≥70 years: https://uit.no/Content/271765/T4_Q2_O70.pdf

Tromsø5 (2001)

- Invitation: https://uit.no/Content/271757/T5_Invitation.pdf
- Consent form: https://uit.no/Content/710358/cache=20203011130454/samtykkerklaering.tromso5.pdf
- Q1 <70 years: https://uit.no/Content/430584/T5_Q1_U70.pdf
- Q1 ≥70 years: https://uit.no/Content/430586/T5_Q1_O70.pdf
- Q2 : https://uit.no/Content/430588/T5_Q2.pdf

Tromsø6 (2007–8)

- Invitation: https://uit.no/Content/100340/Forespoersel_om_deltakelse_t6.pdf
- Consent form: https://uit.no/Content/111929/Samtykke%20Tr6.pdf
- Q1: https://uit.no/Content/401052/Questionnaire_T6_1.pdf
- Q2: https://uit.no/Content/531228/cache=20172908084211/Questionnaire_T6_2.pdf

Tromsø7 (2015–16)

- Invitation: https://uit.no/Content/710341/cache=20203011123325/brosjyre.troms%C3%B87.pdf
- Consent form: https://uit.no/Content/575211/cache=20180805144729/Samtykke.den7.Tromsounderskelsen.pdf
- Q1: https://uit.no/Content/686864/cache=20201407122756/Sporreskjema.Q1.engelskTromso7.pdf
- Q2: https://uit.no/Content/709325/cache=20202011171303/FINAL Q2 translation20190307.pdf

Appendix 2

Selected pages from questionnaires used in Tromsø4 (1994–95) with food-related questions

YOUR OWN HEALTH

What is your current state of health? *Tick one box only.*

Poor	12	1
Not so good		2
Good		3
Very good		4

Do you have, or have you had:

		Yes	No	Age first time
A heart attack	13			years
Angina pectoris (heart cramp)	16			years
A cerebral stroke/ brain haemorrhage	19			years
Asthma	22			years
Diabetes	25			years

Do you use blood pressure lowering drugs?

Currently	28	1
Previously, but not now		2
Never used		3

Have you during the last year suffered from pains and/or stiffness in muscles and joints that have lasted continuously for at least 3 months? 29 — Yes / No

Have you in the last two weeks felt:

		No	A little	A lot	Very much
Nervous or worried?	30				
Anxious?	31				
Confident and calm?	32				
Irritable?	33				
Happy and optimistic?	34				
Down/depressed?	35				
Lonely?	36				
		1	2	3	4

SMOKING

Did any of the adults at home smoke while you were growing up? 37 — Yes / No

Do you currently, or did you previously, live together with daily smokers after your 20th birthday? 38 — Yes / No

If "YES", for how many years in all? 39 — Years

How many hours a day do you normally spend in smoke-filled rooms? 41 — Hours

Put 0 if you do not spend time in smoke-filled rooms.

Do you yourself smoke:

		Yes	No
Cigarettes daily?	43		
Cigars/ cigarillos daily?	44		
A pipe daily?	45		

If you previously smoked daily, how long is it since you quit? 46 — Years

If you currently smoke, or have smoked previously:

How many cigarettes do you or did you usually smoke per day? 48 — cigarettes

How old were you when you began daily smoking? 52 — Age years

How many years in all have you smoked daily? 54 — Years

EXERCISE

How has your physical activity in leisure time been during this last year? *Think of your weekly average for the year.*

Time spent going to work counts as leisure time.

		Hours per week: None	Less than 1	1-2	3 or more
Light activity *(not sweating/out of breath)*	56				
Hard activity *(sweating/ out of breath)*	57				
		1	2	3	4

COFFEE

How many cups of coffee do you drink daily?
Put 0 if you do not drink coffee daily.

Coarsely ground coffee for brewing	58	Cups
Other coffee	60	Cups

ALCOHOL

Are you a teetotaller? 62 — Yes / No

How many times a month do you normally drink alcohol? *Do not count low-alcohol beer.*
Put 0 if less than once a month. 63 — Times

How many glasses of beer, wine or spirits do you normally drink in a fortnight? 65
Do not count low-alcohol beer.
Put 0 if less than once a month.

Beer	Wine	Spirits
Glasses	Glasses	Glasses

FAT

What type of margarine or butter do you usually use on bread? *Tick one box only.*

Don't use butter/margarine	71	1
Butter		2
Hard margarine		3
Soft margarine		4
Butter/margarine mixtures		5
Light margarine		6

EDUCATION/WORK

What is the highest level of education you have completed?

7-10 years primary/secondary school, modern secondary school	72	1
Technical school, middle school, vocational school, 1-2 years senior high school		2
High school diploma (3-4 years)		3
College/university, less than 4 years		4
College/university, 4 or more years		5

What is your current work situation?

Paid work	73	
Full-time housework	74	
Education, military service	75	
Unemployed, on leave without payment	76	

How many hours of paid work do you have per week? 77 — No. of hours

Do you receive any of the following benefits?

Sickness benefit (sick leave)	79	
Rehabilitation benefit	80	
Disability pension	81	
Old-age pension	82	
Social welfare benefit	83	
Unemployment benefit	84	

ILLNESS IN THE FAMILY

Have one or more of your parents or siblings had a heart attack or had angina (heart cramp)? 85 — Yes / No / Don't know

MEDICATION AND DIETARY SUPPLEMENTS

Have you for any length of time in the past year used any of the following medicines or dietary supplements daily or almost daily? Indicate how many months you have used them.
*Put **0** for items you have **not** used.*

Medicines
- Painkillers 215 _____months
- Sleeping pills _____months
- Tranquillizers _____months
- Antidepressants 221 _____months
- Allergy drugs _____months
- Asthma drugs _____months

Dietary supplements
- Iron tablets 227 _____months
- Calcium tablets or bonemeal _____months
- Vitamin D supplements _____months
- Other vitamin supplements 233 _____months
- Cod liver oil or fish oil capsules _____months

Have you in the last 14 days used the following medicines or dietary supplements?
*Tick **one** box only for **each** item.*

	Yes	No
Medicines		
Painkillers 237	☐	☐
Antipyretic drugs (to reduce fever)	☐	☐
Migraine drugs	☐	☐
Eczema cream/ointment	☐	☐
Heart medicines (not blood pressure)	☐	☐
Cholesterol lowering drugs	☐	☐
Sleeping pills	☐	☐
Tranquillizers	☐	☐
Antidepressants	☐	☐
Other drugs for nervous conditions	☐	☐
Antacids 247	☐	☐
Gastric ulcer drugs	☐	☐
Insulin	☐	☐
Diabetes tablets	☐	☐
Drugs for hypothyroidism (Thyroxine)	☐	☐
Cortisone tablets 252	☐	☐
Other medicine(s)	☐	☐
Dietary supplements		
Iron tablets	☐	☐
Calcium tablets or bonemeal	☐	☐
Vitamin D supplements	☐	☐
Other vitamin supplements 257	☐	☐
Cod liver oil or fish oil capsules	☐	☐

FRIENDS

How many good friends do you have whom you can talk confidentially with and who give you help when you need it? 259 _____good friends
Do not count people you live with, but do include other relatives!

How many of these good friends do you have contact with at least once a month? 261 _____

	Yes	No
Do you feel you have enough good friends? 263	☐	☐

How often do you normally take part in organised gatherings, e.g. sewing circles, sports clubs, political meetings, religious or other associations?
- Never, or just a few times a year 264 ☐ 1
- 1-2 times a month ☐ 2
- Approximately once a week ☐ 3
- More than once a week ☐ 4

FOOD HABITS

If you use butter or margarine on your bread, how many slices does a small catering portion normally cover? By this, we mean the portion packs served on planes, in cafés, etc. (10-12g)

A catering portion is enough for about 265 _____slices

What kind of fat is normally used in **cooking** (not on the bread) in your home?
- Butter 266 ☐
- Hard margarine ☐
- Soft margarine ☐
- Butter/margarine blend ☐
- Oils 270 ☐

What kind of bread (bought or home-made) do you usually eat?
Tick one or two boxes!

	White bread	Light textured	Ordinary brown	Coarse brown	Crisp bread
The bread I eat is most similar to:	☐ 271	☐	☐	☐	☐ 275

How much (in **number** of glasses, cups, potatoes or slices) do you usually eat or drink **daily** of the following foodstuffs?
*Tick one box for **each** foodstuff.*

	0	Less than 1	1-2	3-4	5-6	More than 6
Full milk (ordinary or curdled) (glasses) 276	☐	☐	☐	☐	☐	☐
Semi-skimmed milk (ordinary or curdled) (glasses)	☐	☐	☐	☐	☐	☐
Skimmed milk (ordinary or curdled) (glasses)	☐	☐	☐	☐	☐	☐
Tea (cups)	☐	☐	☐	☐	☐	☐
Orange juice (glasses)	☐	☐	☐	☐	☐	☐
Potatoes 281	☐	☐	☐	☐	☐	☐
Slices of bread in total (incl. crisp-bread)	☐	☐	☐	☐	☐	☐
Slices of bread with - fish (e.g. mackerel in tomato sauce)	☐	☐	☐	☐	☐	☐
- lean meat (e.g. ham)	☐	☐	☐	☐	☐	☐
- fat meat (e.g. salami)	☐	☐	☐	☐	☐	☐
- cheese *(e.g. Gouda/ Norvegia)* 286	☐	☐	☐	☐	☐	☐
- brown cheese	☐	☐	☐	☐	☐	☐
- smoked cod caviare	☐	☐	☐	☐	☐	☐
- jam and other sweet spreads	☐	☐	☐	☐	☐	☐
	1	2	3	4	5	6

How many **times per week** do you normally eat the following foodstuffs?
*Tick a box for **all** foodstuffs listed.*

	Never	Less than 1	1	2-3	4-5	almost daily
Yoghurt 290	☐	☐	☐	☐	☐	☐
Boiled or fried egg	☐	☐	☐	☐	☐	☐
Breakfast cereal/ oat meal, etc.	☐	☐	☐	☐	☐	☐
Dinner with - unprocessed meat	☐	☐	☐	☐	☐	☐
- sausage/meatloaf/ meatballs	☐	☐	☐	☐	☐	☐
- fatty fish (e.g. salmon/redfish) 295	☐	☐	☐	☐	☐	☐
- lean fish (e.g. cod)	☐	☐	☐	☐	☐	☐
- fishballs/fishpudding/fishcakes	☐	☐	☐	☐	☐	☐
- vegetables	☐	☐	☐	☐	☐	☐
Mayonnaise, remoulade	☐	☐	☐	☐	☐	☐
Carrots 300	☐	☐	☐	☐	☐	☐
Cauliflower/cabbage/ broccoli	☐	☐	☐	☐	☐	☐
Apples/pears	☐	☐	☐	☐	☐	☐
Oranges, mandarins	☐	☐	☐	☐	☐	☐
Sweetened soft drinks	☐	☐	☐	☐	☐	☐
Sugar-free ("Light") soft drinks	☐	☐	☐	☐	☐	☐
Chocolate	☐	☐	☐	☐	☐	☐
Waffles, cakes, etc. 307	☐	☐	☐	☐	☐	☐
	1	2	3	4	5	6

Appendix 3

Selected pages from questionnaires used in Tromsø5 (2001) with food-related questions

7. FOOD AND BEVERAGES

7.1 How often do you usually eat these foods? *(Tick once per line)*

	Rarely /never	1-3 times /month	1-3 times /week	4-6 times /week	1-2 times /day	3 times or more /day
Fruit, berries	☐	☐	☐	☐	☐	☐
Cheese *(all types)*	☐	☐	☐	☐	☐	☐
Potatoes	☐	☐	☐	☐	☐	☐
Boiled vegetables	☐	☐	☐	☐	☐	☐
Fresh vegetables/salad	☐	☐	☐	☐	☐	☐
Fatty fish *(e.g. salmon, trout, mackerel, herring)*	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

7.2 What type of fat do you usually use? *(Tick once per line)*

	Don't use	Butter	Hard margarine	Soft/light margarine	Oils	Other
On bread	☐	☐	☐	☐	☐	☐
For cooking	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

7.3 Do you use the following dietary supplements:

	Yes, daily	Sometimes	No
Cod liver oil, fish oil capsules	☐	☐	☐
Vitamins and/or mineral supplements?	☐	☐	☐

7.4 How much of the following do you usually drink? *(Tick once per line)*

	Rarely /never	1-6 glasses /week	1 glass /day	2-3 glasses /day	4 glasses or more /day
Full milk, full-fat curdled milk, yoghurt	☐	☐	☐	☐	☐
Semi-skimmed milk, semi-skimmed curdled milk,low-fat yoghurt	☐	☐	☐	☐	☐
Skimmed milk, skimmed curdled milk	☐	☐	☐	☐	☐
Extra semi-skimmed milk	☐	☐	☐	☐	☐
Juice	☐	☐	☐	☐	☐
Water	☐	☐	☐	☐	☐
Mineral water (e.g. Farris, Ramløsa etc)	☐	☐	☐	☐	☐
Cola-containing soft drink	☐	☐	☐	☐	☐
Other soda/soft drink	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

7.5 Do you usually drink soft drink: with sugar ☐ 1 without sugar ☐ 2

7.6 How many cups of coffee and tea do you drink daily? *Number of cups*
(Put 0 for the types you don't drink daily)

Filtered coffee ☐☐

Boiled coffee/coarsely ground coffee for brewing ☐☐

Other type of coffee ☐☐

Tea ☐☐

7.7 Approximately how often have you during the last year consumed alcohol? *(Do not count low-alcohol and alcohol-free beer)*

Never consumed alcohol	Have not consumed alcohol last year	A few times last year	About 1 time a month
☐ 1	☐ 2	☐ 3	☐ 4

2-3 times per month	About1 time a week	2-3 times a week	4-7 times a week
☐ 5	☐ 6	☐ 7	☐ 8

To those who have consumed the last year:

7.8 When you drink alcohol, how many glasses or drinks do you normally drink? *number* ☐☐

7.9 Approximately how many times during the last year have you consumed alcohol equivalent to 5 glasses or drinks within 24 hours? *Number of times* ☐☐

7.10 When you drink, do you normally drink: *(Tick one or more)*

Beer ☐ Wine ☐ Spirits ☐

8. SMOKING

8.1 How many hours a day do you normally spend in smoke-filled rooms? *Number of total hours* ☐☐

	Yes	No
8.2 Did any of the adults smoke at home while you were growing up?	☐	☐
8.3 Do you currently, or did you previously live together with a daily smoker after your 20th birthday?	☐	☐

	Yes, now	Yes, previously	Never
8.4 Do you/did you smoke daily?	☐	☐	☐

If NEVER: Go to question 9 : (EDUCATION AND WORK)

8.5 If you smoke daily now, do you smoke:	Yes	No
Cigarettes?	☐	☐
Cigars/cigarillos?	☐	☐
A pipe?	☐	☐

8.6 If you previously smoked daily, how long is it since you quit? *Number of years* ☐☐

8.7 If you currently smoke, or have smoked previously:

How many cigarettes do you or did you normally smoke per day? *Number of cigarettes* ☐☐

How old were you when you began daily smoking? *Age in years* ☐☐

How many years in all have you smoked daily? *Number of years* ☐☐

9. EDUCATION AND WORK

9.1 How many years of education have you completed? *Number of years* ☐☐
(Include all the years you have attended school or studied)

9.2 Do you currently have paid work?

Yes, full-time ☐ 1 Yes, part-time ☐ 2 No ☐ 3

9.3 Describe the activity at the workplace where you had paid work for the longest period in the last 12 months. *(e.g. Accountancy firm, school, paediatric department, carpentry workshop, garage, bank, grocery store, etc.)*

Business: _____
If retired, enter the former business and occupation. Also applies to 9.4

9.4 Which occupation/title have or had you at this workplace? *(e.g. Secretary, teacher, industrial worker, nurse, carpenter, manager, salesman, driver, etc.)*

Occupation: _____

9.5 In your main occupation, do you work as self-employed, as an employee or family member without regular salary?

Self-employed ☐ Employee ☐ Family member ☐

	Yes	No
9.6 Do you believe that you are in danger of losing your current work or income within the next two years?	☐	☐

9.7 Do you receive any of the following benefits?	Yes	No
Sickness benefit (are on sick leave)	☐	☐
Old age pension, early retirement (AFP) or survivor pension	☐	☐
Rehabilitation/reintegration benefit	☐	☐
Disability pension (full or partial)	☐	☐
Unemployment benefits during unemployment	☐	☐
Social welfare benefits	☐	☐
Transition benefit for single parents	☐	☐

T3. TOBACCO

3.1 Do you smoke?

Yes, daily ☐ 1 Yes, sometimes ☐ 2 No, never ☐ 3

If "Yes, sometimes"

What do you smoke?

☐ Cigarettes ☐ Pipe ☐ Cigar/cigarillos

3.2 Have you used or do you use snuff daily?

Yes, now ☐ Yes, previously ☐ Never ☐

If YES:

How many years altogether have you used snuff? ☐☐ years

T4. ALCOHOL

4.1 Are you a teetotaller? ..... Yes ☐ No ☐

4.2 How many times a month do you normally drink alcohol? ..... ☐☐ *Number of times*

(Do not count low-alcohol beer. Put 0 if less than once a month)

4.3 How many glasses of beer, wine or spirits do you normally drink in a fortnight?

Beer ☐☐ Wine ☐☐ Spirits ☐☐

(Do not count low-alcohol beer. Put 0 if you do not drink alcohol)

4.4 For approximately how many years has your alcohol consumption been at the same level you described above? ☐☐ years

4.5 Have you, in one or more periods in the last 5 years consumed so much alcohol that it has inhibited your work or social life?

Yes, at work ☐ 1 Yes, socially ☐ 2 Yes, both at work and social life ☐ 3 No, never ☐ 4

T5. FOOD AND DIETARY SUPPLEMENTS

5.1 Do you usually eat breakfast every day? ... Yes ☐ No ☐

5.2 How many times a week do you eat a warm dinner? ..... ☐ *times*

5.3 How important is it for you to have a healthy diet?

Very ☐ 1 Somewhat ☐ 2 Little ☐ 3 Not ☐ 4

5.4 Do you use the following dietary supplements?

	Yes, daily	sometimes	No
Iron tablets	☐	☐	☐
Calcium tablets or bonemeal	☐	☐	☐
Vitamin D supplements	☐	☐	☐
Cod liver oil	☐	☐	☐

T6. BODY WEIGHT

6.1 Do you currently try to change your body weight?

No ☐ 1 Yes, I try to gain weight ☐ 2 Yes, I try to lose weight ☐ 3

6.2 What weight would you be satisfied with (your "ideal weight")? ..... ☐☐☐ kg

T7. ILLNESSES AND INJURIES

7.1 Have you ever had:

Tick once for each question. Also give the age at the time. If you have had the condition several times, how old were you the last time

	Yes	No	Age last time
Severe injury requiring hospital admission	☐	☐	☐☐ years
Ankle fracture	☐	☐	☐☐ years
Peptic ulcer	☐	☐	☐☐ years
Peptic ulcer surgery	☐	☐	☐☐ years
Neck surgery	☐	☐	☐☐ years
Prostate surgery	☐	☐	☐☐ years

7.2 Do you have, or have you ever had: *(Tick once for each question)*

	Yes	No
Cancer	☐	☐
Psoriasis.....	☐	☐
Thyroid disease	☐	☐
Glaucoma	☐	☐
Cataract	☐	☐
Osteoarthritis (arthrosis).....	☐	☐
Bent fingers	☐	☐
Skin contractions in your palms	☐	☐
Kidney stone	☐	☐
Appendectomy.....	☐	☐
Hernia surgery	☐	☐
Surgery/treatment for urine incontinence	☐	☐
Epilepsy.....	☐	☐
Poliomyelitis (polio)	☐	☐
Parkinson's disease.....	☐	☐
Migraine.....	☐	☐
Leg ulcer	☐	☐
Allergy and hypersensitivity:	Yes	No
Atopic eczema (e.g. childhood eczema)	☐	☐
Hand eczema.....	☐	☐
Food allergy	☐	☐
Other hypersensitivity (not allergy).....	☐	☐

7.3 Have you had common cold, influenza, gastroenteritis, etc. during the last 14 days? Yes ☐ No ☐

7.4 Have you during the last 3 weeks had common cold, influenza, bronchitis, pneumonia, sinusitis, or other respiratory infection?..... Yes ☐ No ☐

7.5 Have you ever had bronchitis or pneumonia?..... Yes ☐ No ☐

7.6 Have you during the last 2 years had bronchitis or pneumonia? *(Tick only once)*

No ☐ 1 1-2 times ☐ 2 More than 2 times ☐ 3

Appendix 4

Selected pages from questionnaires used in Tromsø6 (2007–08) with food-related questions

DIET

38 **Do you usually eat breakfast every day?**

☐ Yes ☐ No

39 **How many units of fruits or vegetables do you eat on average per day?** (units means for example a fruit, a cup of juice, potatoes, vegetables)

Number of units ☐☐ +

40 **How many times per week do you eat hot dinner?**

Number ☐☐

41 **How often do you usually eat these products?**
(Tick once for each line)

	0-1 times/ mth	2-3 times/ mth	1-3 times/ week	4-6 times/ week	1-2 times/ day
Potatoes	☐	☐	☐	☐	☐
Pasta/rice	☐	☐	☐	☐	☐
Meat *(not processed)*	☐	☐	☐	☐	☐
Processed meat *(sausages/meatloaf/meatballs)*	☐	☐	☐	☐	☐
Fruits, vegetables, berries	☐	☐	☐	☐	☐
Lean fish	☐	☐	☐	☐	☐
Fat fish *(e.g. salmon, trout, mackerel, herring, halibut, redfish)*	☐	☐	☐	☐	☐

42 **How much do you normally drink the following?**
(Tick once for each line)

	Rarely/ never	1-6 glasses /week	1 glass /day	2-3 glasses /day	4 or more glasses /day
Milk, curdled milk, yoghurt	☐	☐	☐	☐	☐
Juice	☐	☐	☐	☐	☐
Soft drinks with sugar	☐	☐	☐	☐	☐

43 **How many cups of coffee and tea do you drink daily?** (Put 0 for the types you do not drink daily)

	Number of cups
Filtered coffee	☐☐
Boiled coffee (coarsely ground coffee for brewing)	☐☐
Other types of coffee	☐☐
Tea	☐☐

44 **How often do you usually eat cod liver and roe?**
(i.e. "mølje")

☐ Rarely/never ☐ 1-3 times/year ☐ 4-6 times/year
☐ 7-12 times/year ☐ More than 12 times/year

45 **Do you use the following supplements?**

	Daily	Sometimes	No
Cod liver oil or fish oil capsules	☐	☐	☐
Omega 3 capsules *(fish oil, seal oil)*	☐	☐	☐
Vitamins and/or mineral supplements	☐	☐	☐

QUESTONS FOR WOMEN

46 **Are you currently pregnant?**

☐ Yes ☐ No ☐ Uncertain

47 **How many children have you given birth to?**

Number ☐☐ +

48 **If you have given birth, fill in for each child: birth year, birth weight and months of breastfeeding** (Fill in the best you can)

Child	Birth year	Birth weight in grams	Months of breastfeeding
1	☐☐☐☐	☐☐☐☐	☐☐
2	☐☐☐☐	☐☐☐☐	☐☐
3	☐☐☐☐	☐☐☐☐	☐☐
4	☐☐☐☐	☐☐☐☐	☐☐
5	☐☐☐☐	☐☐☐☐	☐☐
6	☐☐☐☐	☐☐☐☐	☐☐

49 **During pregnancy, have you had high blood pressure?**

☐ Yes ☐ No

50 **If yes, which pregnancy?**

☐ The first ☐ Second or later

51 **During pregnancy, have you had proteinuria?**

☐ Yes ☐ No

52 **If yes, which pregnancy?**

☐ The first ☐ Second or later

53 **Were any of your children delivered prematurely (a month or more before the due date) because of preeclampsia?**

☐ Yes ☐ No

54 **If yes, which child?**

1st child ☐ 2nd child ☐ 3rd child ☐ 4th child ☐ 5th child ☐ 6th child ☐

55 **How old were you when you started menstruating?**

Age ☐☐ +

56 **Do you currently use any prescribed drug influencing the menstruation?**

Oral contraceptives, hormonal IUD or similar ☐ Yes ☐ No

Hormone treatment for menopausal problems ☐ Yes ☐ No

When attending the survey centre you will get a questionnaire about menstruation and possible use of hormones. Write down on a paper the names of all the hormones you have used and bring the paper with you. You will also be asked whether your menstruation have ceased and possibly when and why.

5. FOOD HABITS

5.01 **How often do you usually eat the following?** (tick once for each line)

	0-1 times per month	2-3 times per month	1-3 times per week	More than 3 times per week
Fresh water fish *(not farmed)*	☐	☐	☐	☐
Salt water fish *(not farmed)*	☐	☐	☐	☐
Farmed fish *(salmon, trout, char)*	☐	☐	☐	☐
Tuna fish *(fresh or canned)*	☐	☐	☐	☐
Fish bread spread	☐	☐	☐	☐
Mussels, shells	☐	☐	☐	☐
The brown content in crabs	☐	☐	☐	☐
Whale or seal meat	☐	☐	☐	☐
Pluck (liver/kidney/heart) from reindeer or elk/moose	☐	☐	☐	☐
Pluck (liver/kidney/heart) from ptarmigan/grouse	☐	☐	☐	☐

5.02 **How many time during the year do/did you usually eat the following?** (number of times)

	In adulthood	In childhood
Mølje (cod or pollack meat, liver, and roe) *(Number of times per year)*		
Gulls egg *(Number of eggs per year)*		
Reindeer meat *(Number of times per year)*		
Local mushroom and wild berries *(blueberries/lingonberries/cloudberries) (Number of times per year)*		

5.03 **How many times per month do you eat canned (tinned) foods (from metal boxes)?**

Number ☐

5.04 **Do you take vitamins and/or mineral supplements?**

☐ Yes, daily ☐ Sometimes ☐ Never

5.05 **How often do you eat?**

	Never	1-3 times per month	1-3 times per week	4-6 times per week	1-2 times per day	3 times per day or more
Dark chocolate	☐	☐	☐	☐	☐	☐
Light chocolate/milk chocolate	☐	☐	☐	☐	☐	☐
Chocolate cake	☐	☐	☐	☐	☐	☐
Other sweets	☐	☐	☐	☐	☐	☐

5.06 **If you eat chocolate, how much do you usually eat each time?**
Compared with the size of a Kvikk-Lunsj sjokolade *(a chocolate brand in the market)* and describe how much do you eat in relation to it.

¼	½	1	1 ½	2	More than 2
☐	☐	☐	☐	☐	☐

5.07 **How often do you drink cocoa/hot chocolate?**

Never	1-3 times per month	1-3 times per week	4-6 times per week	1-2 times per day	3 times per day or more
☐	☐	☐	☐	☐	☐

Appendix 5

Selected pages from questionnaires used in Tromsø7 (2015–16) with food-related questions

USE OF MEDICIN

4.1 **Do you use or have you used?** *Tick once for each line.*

	Never	Now	Previously, not now	Age first time
Blood pressure lowering drugs	☐	☐	☐	☐☐
Cholesterol lowering drugs	☐	☐	☐	☐☐
Diuretics	☐	☐	☐	☐☐
Drugs for heart disease *(for example anticoagulants, antiarrhythmics, nitroglycerin)?*	☐	☐	☐	☐☐
Insulin	☐	☐	☐	☐☐
Tablets for diabetes	☐	☐	☐	☐☐
Drugs for hypothyroidism (Levaxin or thyroxine)?	☐	☐	☐	☐☐

4.2 **How often during the past four weeks have you used?** *Tick once for each line.*

	Not used in the past 4 weeks	Less than every week	Every week but not daily	Daily
Painkillers on prescription	☐	☐	☐	☐
Painkiller non-prescription	☐	☐	☐	☐
Acid suppressive medication	☐	☐	☐	☐
Sleeping pills	☐	☐	☐	☐
Tranquillizers	☐	☐	☐	☐
Antidepressants	☐	☐	☐	☐

4.3 **State the name of all medicines, both those on prescription and non-prescription drugs, you have used regularly during the last 4 weeks.** *Do not include nonprescription vitamin-, mineral- and food supplements, herbs, naturopathic remedies etc.*

If there is not enough space for all medicines, continue on a separate sheet.

DIET

5.1 **Do you usually eat breakfast every day?**

☐ No ☐ Yes

5.2 **How many units of fruit or vegetables do you eat on average per day?** *One unit is by example one apple, one salad bowl.*

Number of units ☐☐

5.3 **How often do you eat these food items?** *Tick once for each line.*

	0–1 times per month	2–3 times per month	1–3 times per week	4–6 times per week	Once a day or more
Red meat *(All products from beef, mutton, pork)?*	☐	☐	☐	☐	☐
Fruits, vegetables, and berries?	☐	☐	☐	☐	☐
Lean fish *(Cod, Saithe)?*	☐	☐	☐	☐	☐
Fat fish *(salmon, trout, redfish, mackerel, herring, halibut)?*	☐	☐	☐	☐	☐

5.4 **How many glasses / containers of the following do you normally drink / eat?** *Tick once for each line.*

	Rarely / never	1–6 glasses per week	1 glass per day	2–3 glass per day	4 or more per day
Milk / Yogurt with probiotics (Biola, Cultura, Activia, Actimel, BioQ etc.)	☐	☐	☐	☐	☐
Fruit juice	☐	☐	☐	☐	☐
Soft drinks with sugar	☐	☐	☐	☐	☐
Soft drinks with artificial sweeteners	☐	☐	☐	☐	☐

5.5 **How many cups of coffee or tea do you usually drink daily?** *Put 0 for the types you <u>do not</u> drink daily.*

	Number of cups
Filtered coffee	☐☐
Boiled coffee / french plunger coffee *(coarsely ground coffee for brewing)*	☐☐
Instant coffee	☐☐
Cups of espresso-based coffee *(from coffee-machines, capsules etc.)*	☐☐
Black tea *(e.g. Earl Grey, Black currant)*	☐☐
Green tea / white tea / oolong tea	☐☐
Herbal tea *(e.g. rose hip tea, chamomile tea, Rooibos tea)*	☐☐

15-29 minutes

30-60 minutes

More than 1 hour

20 FOOD HABITS

How often do you usually eat?

Tick once for each line

	0-1 times per month	2-3 times per month	1-3 times per week	More than 3 times per week
20.1 Fresh water fish (not farmed)				
20.2 Salt water fish (not farmed)				
20.3 Farmed fish (salmon, trout, char)				
20.4 Tuna fish (fresh or canned)				
20.5 Fish bread spread				
20.6 Mussels, shells				
20.7 Brown content in crabs				
20.8 Meat from whale or seal				
20.9 Pluck (liver/kidney/heart) from reindeer or elk/moose				
20.10 Pluck (liver/kidney/heart) from ptarmigan/grouse				
20.11 Tomatoes and tomato-based products (e.g. tomato, ketchup)				

How many times per year do/did you usually eat

	In adulthood: times per year	In childhood: times per year
20.12 "Mølje" (cod or pollack meat, liver, and roe)		
20.13 Seagulls' egg		
20.14 Reindeer meat		
20.15 Elk meat		
20.16 Wild mushroom and wild berries (blueberries/lingonberries/cloudberries)		

Do you use the following food supplements?

(Tick once for each line)

	No	Sometimes	Daily during the winter season	Daily
20.17 Cod liver oil or cod liver oil capsules				
20.18 Omega 3 capsules (fish oil, seal oil)				
20.19 Calsium tablets				
20.20 Vitamin supplement with vitamin D				

	No	Sometimes	Only while travelling	Daily

Appendix 6

Food frequency questionnaire in Tromsø7 (2015–16)

UiT
NORGES
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UNIVERSITET

Tromsø-
undersøkelsen

Spørreskjema om kosthold

Utfylte svar i spørreskjema er like viktig for Tromsøundersøkelsen som resultater fra blodprøver og kliniske undersøkelser.

Forskere har funnet ut at kosthold er den risikofaktoren som fører til flest tapte leveår og dager med sykdom eller skade i Norge. Det finnes lite informasjon om kostholdet i Nord-Norge. Vi ber deg derfor fylle ut dette spørreskjemaet som vil gi viktige data for forskningen.

Vi spør her om matvanene dine og hvor ofte du vanligvis spiser og drikker ulike typer mat og drikke. Vi er klar over at kostholdet varierer fra dag til dag, men prøv så godt du kan å gi et «gjennomsnitt» av matvanene dine. Ha det siste året i tankene når du fyller ut skjemaet. Der du er usikker anslår du svaret ditt.

Alle svar lagres og behandles uten navn og fødselsnummer, i samsvar med lover og forskrifter.

Dersom du fyller ut skjemaet hjemme, bruk vedlagte svarkonvolutt.

Takk for at du tar deg tid til å fylle ut skjemaet.

UiO : Det medisinske fakultet

UNIVERSITETET I TROMSØ

Skjemaet skal lese av en maskin og det er derfor viktig at du setter tydelige kryss i rutene. Bruk blå eller sort kulepenn.

☒ Riktig markering i rutene er slik
■ Ved feil markering, fyll hele ruten slik

Har du spørsmål om utfyllingen av skjemaet kan du ta kontakt med personalet på undersøkelsen eller sende e-post til: tromso7@ism.uit.no

Eksempel

Kari Normann spiser daglig 5 skiver brød og ett grovt knekkebrød. Hun spiser vanligvis kneippbrød, men i helgene spiser hun som oftest loff. Spørsmål 1 fyller hun ut slik:

1. Hvor mye brød pleier du å spise?

Legg sammen det du bruker til alle måltider i løpet av en dag.
(1/2 rundstykke = 1 skive, 1 baguett = 4 skiver, 1 ciabatta = 2 skiver)

	Aldri/ sjelden	Antall skiver pr. dag ½	1	2	3	4	5	6	7	8	9	10	11	12+
Fint brød (loff, baguetter, fine rundstykker, ciabatta)	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Mellomgrovt brød (helkornbrød, kneipp, grove rundstykker)	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐
Grovt brød (mer enn 50 % sammalt, mørkt rugbrød)	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Fint knekkebrød (kavring)	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Grovt knekkebrød (grov skonrok)	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Sum skiver pr. dag = 6

Antall skiver pr. uke: 6 x 7 = 42. Tallet brukes i spørsmål 4.

Prøv så godt du kan å gi et «gjennomsnitt» av matvanene dine.
Ha det siste året i tankene når du fyller ut.

1. Hvor mye brød pleier du å spise?

Legg sammen det du bruker til alle måltider i løpet av en dag.
(1/2 rundstykke = 1 skive, 1 baguett = 4 skiver, 1 ciabatta = 2 skiver)

	Aldri / sjelden	Antall skiver pr. dag ½	1	2	3	4	5	6	7	8	9	10	11	12+
Fint brød (loff, baguetter, fine rundstykker, ciabatta)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Mellomgrovt brød (helkornbrød, kneipp, grove rundstykker)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Grovt brød (mer enn 50 % sammalt, mørkt rugbrød)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Fint knekkebrød (kavring)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Grovt knekkebrød (grov skonrok)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Sum skiver pr. dag = _____

Antall skiver pr. uke: _____ x 7 = _____. Tallet brukes i spørsmål 4.
(sum skriver pr. dag)

2. Hva pleier du å smøre på brødet?

Legg sammen det du bruker på skivene i løpet av en uke.
(1/2 rundstykke = 1 skive, 1 baguett = 4 skiver, 1 ciabatta = 2 skiver)

	Aldri / sjelden	Antall skiver pr. uke 1-5	6-14	15-21	22-28	29-35	36-42	43-49	50-56	57+
Smør (meierismør)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Bremykt	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Brelett	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Myk margarin (Soft Flora, Soft Ekstra)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Vita	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Soft Light, Vita Lett	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Melange	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Annen margarin	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Olivenolje, annen olje på brød	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Majones, remulade på brød	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

3. Hvis du bruker smør / margarin på brødet, hvor mye bruker du?

	Antall skiver ½	1	2	3	4	5 eller flere
En porsjonspakke smør/margarin på 12 g rekker til antall skiver:	☐	☐	☐	☐	☐	☐

Prøv så godt du kan å gi et «gjennomsnitt» av matvanene dine.
Ha det siste året i tankene når du fyller ut.

4. Hvilke typer pålegg spiser du?

	Aldri/ sjelden	Antall skiver pr. uke								
		1	2-3	4-5	6-7	8-12	13-18	19-24	25-30	31+
Brunost/prim	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Lett/mager brunost/prim	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Hvitost (eks. Norvegia, Gulost)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Lett/mager hvitost	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Dessertost (eks. Brie, Gräddost, blåmuggoster)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Smøreost (eks. kremost, Philadelfia)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Lett/mager smøreost	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Leverpostei	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Mager leverpostei	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Servelat	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Kokt skinke, lettservelat, kalkunpålegg	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Salami, fårepølse, spekepølse	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Kaviar	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Svolværpostei, Lofotpostei	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Makrell i tomat	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Røkt, gravet laks/ørret	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Sardiner, sursild, ansjos	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Tunfisk	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Reker, krabbe	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Egg (kokt, stekt, eggerøre)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Syltetøy, marmelade	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Lett syltetøy, frysetøy	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Peanøttsmør	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Sjokolade-, nøttepålegg	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Annet søtt pålegg (eks. honning, Sunda, sirup)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Cottage cheese	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Majonessalat (eks. italiensk salat)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Majonessalat lett (eks. lett italiensk salat)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Frukt som pålegg (eks. banan, eple)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Grønnsaker som pålegg (eks. agurk, tomat)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Prøv så godt du kan å gi et «gjennomsnitt» av matvanene dine.
Ha det siste året i tankene når du fyller ut.

5. Frokostgryn

Svar enten per måned eller per uke.

	Aldri/ sjelden	Gang pr. måned 1	2	3	eller	Gang pr. uke 1	2-3	4-5	6-7	8+		Mengde pr. gang 1	1½	2	3+
Havregrøt	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Havregryn, 4-korn	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Mysli, søtet (eks. Solfrokost)	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Mysli, usøtet (eks. Go'Dag)	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Cornflakes	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Honnikorn/Frosties/Chocofrokost	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
All Bran, Weetabix, Havrefras o.l.	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Puffet ris, havrenøtter	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
	Aldri/ sjelden	**Gang pr. måned 1**	**2**	**3**	**eller**	**Gang pr. uke 1**	**2-3**	**4-5**	**6-7**	**8+**		**Mengde pr. gang 1**	**1½**	**2**	**3+**
Syltetøy til frokostgryn, grøt	☐	☐	☐	☐		☐	☐	☐	☐	☐	(ss)	☐	☐	☐	☐
Sukker til frokostgryn, grøt	☐	☐	☐	☐		☐	☐	☐	☐	☐	(ts)	☐	☐	☐	☐

6. Melk (Husk også å ta med melk du bruker på frokostgryn, grøt og dessert)

(1 glass = 2 dl)

	Aldri/ sjelden	Antall glass pr. dag ½	1	2	3	4	5	6	7+
Helmelk, kefir, kultur	☐	☐	☐	☐	☐	☐	☐	☐	☐
Lettmelk	☐	☐	☐	☐	☐	☐	☐	☐	☐
Ekstra lettmelk	☐	☐	☐	☐	☐	☐	☐	☐	☐
Skummet melk, skummet kultur	☐	☐	☐	☐	☐	☐	☐	☐	☐
Biola/Cultura naturell	☐	☐	☐	☐	☐	☐	☐	☐	☐
Biola/Cultura med bær/frukt	☐	☐	☐	☐	☐	☐	☐	☐	☐
Sjokolademelk, jordbærmelk	☐	☐	☐	☐	☐	☐	☐	☐	☐
Drikkeyoghurt	☐	☐	☐	☐	☐	☐	☐	☐	☐

7. Yoghurt (Husk å ta med yoghurt du bruker til frokostgryn)

Svar enten per måned eller per uke.

	Aldri/ sjelden	Gang pr. måned 1	2	3	eller	Gang pr. uke 1	2-3	4-5	6-7	8+	Beger pr. gang ½	1	2	3+
Yoghurt naturell (125 g)	☐	☐	☐	☐		☐	☐	☐	☐	☐	☐	☐	☐	☐
Yoghurt med frukt (125 g)	☐	☐	☐	☐		☐	☐	☐	☐	☐	☐	☐	☐	☐
Go'morgen yoghurt m/mysli	☐	☐	☐	☐		☐	☐	☐	☐	☐	☐	☐	☐	☐
Lettyoghurt med frukt (125 g)	☐	☐	☐	☐		☐	☐	☐	☐	☐	☐	☐	☐	☐
Lettyoghurt m/mysli	☐	☐	☐	☐		☐	☐	☐	☐	☐	☐	☐	☐	☐

Prøv så godt du kan å gi et «gjennomsnitt» av matvanene dine.
Ha det siste året i tankene når du fyller ut.

8. Kalde drikker

Svar enten per uke eller per dag, <1 betyr sjeldnere enn 1 gang. Merk at porsjonsenhetene er forskjellige, 1/5 liter tilsvarer ett glass (2 dl), mens 1/3 liter tilsvarer 0,33 liter glassflaske/boks.

	Aldri / sjelden	Gang pr. uke <1	1-2	3-4	5-6	eller	Gang pr. dag 1	2	3	4+	Mengde pr. gang				
Vann (springvann)	☐	☐	☐	☐	☐		☐	☐	☐	☐	(glass)	1 ☐	2 ☐	3 ☐	4+ ☐
Flaskevann med/uten kullsyre (eks. Farris, Imsdal)	☐	☐	☐	☐	☐		☐	☐	☐	☐	(liter)	1/5 ☐	1/3 ☐	½ ☐	1+ ☐
Appelsinjuice	☐	☐	☐	☐	☐		☐	☐	☐	☐	(glass)	1 ☐	2 ☐	3 ☐	4+ ☐
Eplejuice, annen juice	☐	☐	☐	☐	☐		☐	☐	☐	☐	(glass)	1 ☐	2 ☐	3 ☐	4+ ☐
Eplenektar, annen nektar	☐	☐	☐	☐	☐		☐	☐	☐	☐	(glass)	1 ☐	2 ☐	3 ☐	4+ ☐
Saft med sukker	☐	☐	☐	☐	☐		☐	☐	☐	☐	(glass)	1 ☐	2 ☐	3 ☐	4+ ☐
Saft, kunstig søtet	☐	☐	☐	☐	☐		☐	☐	☐	☐	(glass)	1 ☐	2 ☐	3 ☐	4+ ☐
Brus med sukker	☐	☐	☐	☐	☐		☐	☐	☐	☐	(liter)	1/5 ☐	1/3 ☐	½ ☐	1+ ☐
Brus, kunstig søtet	☐	☐	☐	☐	☐		☐	☐	☐	☐	(liter)	1/5 ☐	1/3 ☐	½ ☐	1+ ☐
Iste med sukker	☐	☐	☐	☐	☐		☐	☐	☐	☐	(liter)	1/5 ☐	1/3 ☐	½ ☐	1+ ☐
Iste, kunstig søtet	☐	☐	☐	☐	☐		☐	☐	☐	☐	(liter)	1/5 ☐	1/3 ☐	½ ☐	1+ ☐
Alkoholfritt øl (eks. Vørterøl, Munkholm)	☐	☐	☐	☐	☐		☐	☐	☐	☐	(liter)	1/5 ☐	1/3 ☐	½ ☐	1+ ☐

9. Alkoholholdige drikker

Svar enten pr. måned eller pr. uke. Merk at porsjonsenhetene er forskjellige, 1/5 liter tilsvarer ett glass (2 dl), mens 1/3 liter tilsvarer 0,33 liter glassflaske/boks.

	Aldri / sjelden	Gang pr. måned 1	2	3	eller	Gang pr. uke 1	2-3	4-5	6-7	Mengde pr. gang						
Øl, sterk øl, pils	☐	☐	☐	☐		☐	☐	☐	☐	(liter)	1/3 ☐	½ ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Lettøl	☐	☐	☐	☐		☐	☐	☐	☐	(liter)	1/3 ☐	½ ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Rusbrus, Cider m/alkohol	☐	☐	☐	☐		☐	☐	☐	☐	(liter)	1/5 ☐	1/3 ☐	½ ☐	1 ☐	1½ ☐	2+ ☐
Rødvin	☐	☐	☐	☐		☐	☐	☐	☐	(vinglass)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6+ ☐
Hvitvin	☐	☐	☐	☐		☐	☐	☐	☐	(vinglass)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6+ ☐
Hetvin (portvin, sherry o.l.)	☐	☐	☐	☐		☐	☐	☐	☐	(1 glass = 4cl)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6+ ☐
Brennevin, likør	☐	☐	☐	☐		☐	☐	☐	☐	(1 dram = 4cl)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6+ ☐
Blandede drinker, cocktail	☐	☐	☐	☐		☐	☐	☐	☐	(drink)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6+ ☐

Prøv så godt du kan å gi et «gjennomsnitt» av matvanene dine.
Ha det siste året i tankene når du fyller ut.

10. Varme drikker

Svar enten per uke eller per dag, < 1 betyr sjeldnere enn 1 gang.

	Aldri/ sjelden	Gang pr. uke <1	1-2	3-4	5-6	eller 1	Gang pr. dag 2	3	4+	Mengde pr. gang (kopp) 1	2	3-4	5-6	7-8	9+
Kaffe - kokt og presskanne *1 kopp = 2 dl*	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Kaffe - traktet, filter *1 kopp = 2 dl*	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Kaffe - pulver (instant) *1 kopp = 2 dl*	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Espresso *1 kopp = 0,3 dl*	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Caffe latte *1 kopp = 3 dl*	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Cappucino *1 kopp = 3 dl*	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Kakao/varm sjokolade *1 kopp = 2 dl*	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Sort te (eks. Earl Grey, solbær) *1 kopp = 2 dl*	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Grønn te *1 kopp = 2 dl*	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Urtete (eks. nype, kamille, Rooibois) *1 kopp = 2 dl*	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

	Bruker ikke	Antall pr. kopp ½	1	2	3	4+
Sukker til te (ts/sukkerbit)	☐	☐	☐	☐	☐	☐
Sukker til kaffe (ts/sukkerbit)	☐	☐	☐	☐	☐	☐
Sukketter til te (stk)	☐	☐	☐	☐	☐	☐
Sukketter til kaffe (stk)	☐	☐	☐	☐	☐	☐
Melk/fløte til te (ss)	☐	☐	☐	☐	☐	☐
Melk/fløte til kaffe (ss)	☐	☐	☐	☐	☐	☐

Prøv så godt du kan å gi et «gjennomsnitt» av matvanene dine.
Ha det siste året i tankene når du fyller ut.

11. Middagsretter

Vi spør både om middagsmåltidene og det du spiser til andre måltider. Legg til slutt sammen hvor mange retter per måned du har merket av for å se om summen virker sannsynlig.

	Aldri/ sjelden	Gang pr. måned 1	2	3	4	5-6	7-8	9+	Mengde pr. gang					
Kjøtt/kjøttretter														
Kjøttpølse av storfe/svin	☐	☐	☐	☐	☐	☐	☐	☐	(pølse)	½ ☐	1 ☐	1½ ☐	2 ☐	3+ ☐
Kjøttpølse av storfe/svin, lett/mager	☐	☐	☐	☐	☐	☐	☐	☐	(pølse)	½ ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Kjøttpølse av kylling/kalkun	☐	☐	☐	☐	☐	☐	☐	☐	(pølse)	½ ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Grillpølse/wienerpølse av storfe/svin	☐	☐	☐	☐	☐	☐	☐	☐	(pølse)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Grillpølse/wienerpølse av kylling/kalkun	☐	☐	☐	☐	☐	☐	☐	☐	(pølse)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Hamburger (m/brød)	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Karbonade	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Kjøttkaker, medisterkaker, kjøttpudding	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Kjøttsaus, gryterett med kjøttdeig	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Taco (tacoskjell med kjøtt og salat)	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Tortilla lefse (med kjøtt og salat)/ wrap	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Kebab	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	½ ☐	1 ☐	1½ ☐	2 ☐	3+ ☐
Lasagne, moussaka	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Pizza (en Grandiosa = ca 550 g)	☐	☐	☐	☐	☐	☐	☐	☐	(pizza)	1/8 ☐	1/4 ☐	½ ☐	3/4 ☐	1+ ☐
Calzone (1 stk = 250-300 g)	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	½ ☐	1 ☐	1½ ☐	2 ☐	2½+ ☐
Pai/quiche	☐	☐	☐	☐	☐	☐	☐	☐	(bit)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Vårruller	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Biff (svin, okse, lam)	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	½ ☐	1 ☐	1½ ☐	2 ☐	2½+ ☐
Koteletter (svin, okse, lam)	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	½ ☐	1 ☐	1½ ☐	2 ☐	2½+ ☐
Stek (svin, okse, lam)	☐	☐	☐	☐	☐	☐	☐	☐	(skive)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Stek (elg, hjort, reinsdyr, rådyr)	☐	☐	☐	☐	☐	☐	☐	☐	(skive)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Gryterett med helt kjøtt, frikassé, fårikål	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Lapskaus, suppelapskaus, betasuppe	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐

Middagsretter fortsetter neste side.....

Prøv så godt du kan å gi et «gjennomsnitt» av matvanene dine.
Ha det siste året i tankene når du fyller ut.

Middagsretter forts...

	Aldri/ sjelden	Gang pr. måned 1	2	3	4	5-6	7-8	9+	Mengde pr. gang					
Kjøtt/kjøttretter forts...										1-2	3-4	5-6	7-8	9+
Bacon, stekt flesk	☐	☐	☐	☐	☐	☐	☐	☐	(skive)	☐	☐	☐	☐	☐
										1/4	1/3	1/2	3/4	1+
Grillet kylling	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐	☐
										½	1	1½	2	3+
Kyllingfilet	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐	☐
										1	2	3	4	5+
Wok med kjøtt/kylling og grønnsaker	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐	☐
										1-2	3-4	5-6	7-8	9+
Kyllinggryte	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐	☐
Fisk/fiskeretter														
										1	2	3	4	5+
Fiskekaker, fiskepudding	☐	☐	☐	☐	☐	☐	☐	☐	(kake)	☐	☐	☐	☐	☐
										1-2	3-4	5-6	7-9	10+
Fiskeboller	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐	☐
										1	2	3	4	5+
Torsk, sei, hyse, steinbit, uer (kokt)	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐	☐
										1	2	3	4	5+
Torsk, sei, hyse, steinbit, uer (stekt, panert)	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐	☐
										1-2	3-4	5-6	7-9	10+
Fiskepinner	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐	☐
										1	2	3	4	5+
Sild (fersk, speket, røkt)	☐	☐	☐	☐	☐	☐	☐	☐	(filet)	☐	☐	☐	☐	☐
										½	1	1½	2	3+
Makrell (fersk, røkt)	☐	☐	☐	☐	☐	☐	☐	☐	(filet)	☐	☐	☐	☐	☐
										1	2	3	4	5+
Laks, ørret (kokt, stekt)	☐	☐	☐	☐	☐	☐	☐	☐	(skive)	☐	☐	☐	☐	☐
										1-2	3-4	5-6	7-8	9+
Fiskegryte, fiskesuppe	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐	☐
										1-2	3-4	5-6	7-8	9+
Fiskegrateng	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐	☐
										1	2	3	4	5+
Reker, krabbe	☐	☐	☐	☐	☐	☐	☐	☐	(dl, renset)	☐	☐	☐	☐	☐
										1-2	3-4	5-6	7-8	9+
Wok med sjømat og grønnsaker	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐	☐
Annet														
										1-2	3-4	5-6	7-8	9+
Rømmegrøt	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐	☐
										1-2	3-4	5-6	7-8	9+
Risengrynsgrøt, annen melkegrøt	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐	☐
										1-2	3-4	5-6	7-8	9+
Pannekaker	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐	☐
										1-2	3-4	5-6	7-8	9+
Suppe (tomat, blomkål, ertesuppe)	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐	☐
										1-2	3-4	5-6	7-8	9+
Vegetarrett, vegetarpizza, grønnsaksgrateng	☐	☐	☐	☐	☐	☐	☐	☐	(bit/dl)	☐	☐	☐	☐	☐
										½	1	1½	2	3+
Hurtignudler (eks. Mr Lee)	☐	☐	☐	☐	☐	☐	☐	☐	(pakke)	☐	☐	☐	☐	☐
										1	2	3	4	5+
Omelett	☐	☐	☐	☐	☐	☐	☐	☐	(av antall egg)	☐	☐	☐	☐	☐

Prøv så godt du kan å gi et «gjennomsnitt» av matvanene dine.
Ha det siste året i tankene når du fyller ut.

12. Poteter, ris, spagetti, grønnsaker

Svar enten per måned eller per uke.
Disse spørsmålene dreier seg først og fremst om tilbehør til middagsretter, men spiser du for eksempel en rå gulrot eller salat til lunsj, skal det tas med her.

	Aldri/ sjelden	Gang pr. måned 1	2	3	eller	Gang pr. uke 1	2-3	4-5	6-7	8+		Mengde pr. gang				
Poteter, kokte og bakte	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Potetmos	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Potetsalat m/majones	☐	☐	☐	☐		☐	☐	☐	☐	☐	(ss)	1 ☐	2-3 ☐	4-5 ☐	6-7 ☐	8+ ☐
Fløtegratinerte poteter	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Stekte poteter	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Pommes frites (gatekjøkken, frityrstekt)	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Pommes frites, varmet i ovn	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Bønner/linser	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Ris	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Spagetti, makaroni, pasta	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Pølsebrød, lomper	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Gulrot	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Hodekål	☐	☐	☐	☐		☐	☐	☐	☐	☐	(skalk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Kålrot	☐	☐	☐	☐		☐	☐	☐	☐	☐	(skive)	1/2 ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Blomkål	☐	☐	☐	☐		☐	☐	☐	☐	☐	(hode)	1/8 ☐	1/6 ☐	1/4 ☐	1/3 ☐	1/2+ ☐
Brokkoli	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	1/8 ☐	1/4 ☐	1/2 ☐	3/4 ☐	1+ ☐
Rosenkål	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Løk, rå og stekt	☐	☐	☐	☐		☐	☐	☐	☐	☐	(ss)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Salat (eks. issalat, ruccola)	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	1/2 ☐	1 ☐	1 1/2 ☐	2 ☐	2 1/2+ ☐
Paprika	☐	☐	☐	☐		☐	☐	☐	☐	☐	(ring)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Avokado	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	1/4 ☐	1/2 ☐	3/4 ☐	1 ☐	1 1/2+ ☐
Tomat	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	1/2 ☐	1 ☐	1 1/2 ☐	2 ☐	2 1/2+ ☐
Mais	☐	☐	☐	☐		☐	☐	☐	☐	☐	(ss)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Frosne grønnsakblandinger	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Blandet salat (eks. salat, tomat, agurk, mais)	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐

Prøv så godt du kan å gi et «gjennomsnitt» av matvanene dine.
Ha det siste året i tankene når du fyller ut.

13. Saus og dressing

	Aldri / sjelden	Gang pr. måned: 1	2	3	4	5-6	7-8	9+	Mengde pr. gang					
Brun/hvit saus	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	½ ☐	1 ☐	1½ ☐	2 ☐	3+ ☐
Bearnéssaus, hollandés	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	½ ☐	1 ☐	1½ ☐	2 ☐	3+ ☐
Smeltet margarin/smør	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	½ ☐	1 ☐	1½ ☐	2 ☐	3+ ☐
Kryddersmør	☐	☐	☐	☐	☐	☐	☐	☐	(ts)	½ ☐	1 ☐	1½ ☐	2 ☐	3+ ☐
Majones/remulade vanlig	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	½ ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Majones/remulade lett	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	½ ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Seterrømme (35 % fett)	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	½ ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Lettrømme (20 % fett)	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	½ ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Ekstra lett rømme (10 % fett)	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	½ ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Dressing (eks. Thousand Island)	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	½ ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Lett dressing (eks. lett Thousand Island)	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	½ ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Oljedressing, vinagrette	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	½ ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Soyasaus	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	½ ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Pesto	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	½ ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Tomatsaus, salsa	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Ketchup	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	½ ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Sennep	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	½ ☐	1 ☐	2 ☐	3 ☐	4+ ☐

14. Hvilken type smør / margarin / olje bruker du mest til matlaging?

(Velg en eller to typer)

Smør / margarin	Oljer
☐ Smør (meierismør)	☐ Olivenolje
☐ Bremykt	☐ Soyaolje
☐ Melange	☐ Maisolje
☐ Soft Flora, Soft Ekstra	☐ Solsikkeolje
☐ Vita	☐ Valnøttolje
☐ Flytende margarin på flaske (Vita, Melange, Bremykt o.l.)	☐ Rapsolje
☐ Annen margarin	☐ Vita hjertego
	☐ Andre oljer

Prøv så godt du kan å gi et «gjennomsnitt» av matvanene dine.
Ha det siste året i tankene når du fyller ut.

15. Frukt

Svar enten per måned eller per uke.

	Aldri/ sjelden	Gang pr. måned 1	2	3	eller 1	Gang pr. uke 2-3	4-5	6-7	8+		Mengde pr. gang			
Eple	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Pære	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Banan	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Appelsin	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Klementiner	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4+ ☐
Grapefrukt	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Fersken, nektarin	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4+ ☐
Kiwi	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4+ ☐
Druer	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1-10 ☐	11-20 ☐	21-40 ☐	41+ ☐
Melon	☐	☐	☐	☐	☐	☐	☐	☐	☐	(skive)	1 ☐	2 ☐	3 ☐	4+ ☐
Jordbær (friske, frosne)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Bringebær (friske, frosne)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Blåbær	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Multer	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Rosiner	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Tørket frukt (eks. aprikos, fiken)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1-5 ☐	6-10 ☐	11-15 ☐	16+ ☐
Frukt- og nøtteblanding	☐	☐	☐	☐	☐	☐	☐	☐	☐	(neve)	1 ☐	2 ☐	3 ☐	4+ ☐

16. Grønnsaker og frukt

Hvor mange porsjoner grønnsaker (utenom potet) spiser du vanligvis pr. dag? (En porsjon er f. eks. 1 gulrot, 1 bolle salat)

Mindre enn 1 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5+ ☐

Hvor mange frukt spiser du vanligvis pr. dag?

Mindre enn 1 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5+ ☐

Prøv så godt du kan å gi et «gjennomsnitt» av matvanene dine.
Ha det siste året i tankene når du fyller ut.

17. Desserter, kaker, godteri

Svar enten per måned eller per uke.

	Aldri/ sjelden	Gang pr. måned 1	2	3	eller	Gang pr. uke 1	2-3	4-5	6-7	8+		Mengde pr. gang			
Iskrem (1 dl=1 pinne=1 kremmerhus)	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	☐ 1/2	☐ 1	☐ 2	☐ 3+
Saftis/sorbet (1 dl=1 pinne)	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	☐ 1/2	☐ 1	☐ 2	☐ 3+
Hermetisk frukt, fruktgrøt	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	☐ 1	☐ 2	☐ 3	☐ 4+
Frisk fruktsalat	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	☐ 1	☐ 2	☐ 3	☐ 4+
Pudding (eks. sjokolade, karamell)	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	☐ 1	☐ 2	☐ 3	☐ 4+
Vaniljesaus	☐	☐	☐	☐		☐	☐	☐	☐	☐	(dl)	☐ 1/2	☐ 1	☐ 2	☐ 3+
Pisket krem	☐	☐	☐	☐		☐	☐	☐	☐	☐	(ss)	☐ 1	☐ 2	☐ 3	☐ 4+
Boller, julekake, kringle	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	☐ 1/2	☐ 1	☐ 2	☐ 3+
Skolebrød, skillingsbolle	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	☐ 1/2	☐ 1	☐ 2	☐ 3+
Wienerbrød, -kringle	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	☐ 1/2	☐ 1	☐ 2	☐ 3+
Muffins, formkake	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	☐ 1/2	☐ 1	☐ 2	☐ 3+
Vafler	☐	☐	☐	☐		☐	☐	☐	☐	☐	(plate)	☐ 1/2	☐ 1	☐ 2	☐ 3+
Lefse, påsmurt	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	☐ 1/2	☐ 1	☐ 2	☐ 3+
Sjokoladekake, brownie	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	☐ 1/2	☐ 1	☐ 2	☐ 3+
Marsipankake, bløtkake	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	☐ 1/2	☐ 1	☐ 2	☐ 3+
Søt kjeks, kakekjeks (eks. Cookies, Bixit, Hob Nobs)	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	☐ 1-2	☐ 3-4	☐ 5-6	☐ 7+
Kokosbolle	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	☐ 1	☐ 2	☐ 3	☐ 4+
Sjokolade (60 g) (eks. melkesjokolade, snickers)	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	☐ 1/2	☐ 1	☐ 2	☐ 3+
Mørk sjokolade (70% kakao)	☐	☐	☐	☐		☐	☐	☐	☐	☐	(biter)	☐ 1-3	☐ 4-6	☐ 7-9	☐ 10+
Sjokoladebiter/konfekt	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	☐ 1-3	☐ 4-6	☐ 7-9	☐ 10+
Pastiller uten sukker	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	☐ 1-3	☐ 4-6	☐ 7-9	☐ 10+
Drops, pastiller, lakris, seigmenn	☐	☐	☐	☐		☐	☐	☐	☐	☐	(stk)	☐ 1-3	☐ 4-6	☐ 7-9	☐ 10+
Smågodt (1 hg = 100g)	☐	☐	☐	☐		☐	☐	☐	☐	☐	(hg)	☐ 1/2	☐ 1	☐ 2	☐ 3+
Potetgull	☐	☐	☐	☐		☐	☐	☐	☐	☐	(neve)	☐ 1-2	☐ 3-5	☐ 6-10	☐ 11+
Annen snacks (skruer, crisp, saltstenger, lettsnacks o.l.)	☐	☐	☐	☐		☐	☐	☐	☐	☐	(neve)	☐ 1-2	☐ 3-5	☐ 6-10	☐ 11+
Peanøtter, cashewnøtter (1 neve = 25 gram)	☐	☐	☐	☐		☐	☐	☐	☐	☐	(neve)	☐ 1-2	☐ 3-4	☐ 5-6	☐ 7+
Mandler, hasselnøtter, valnøtter (1 neve = 25 gram)	☐	☐	☐	☐		☐	☐	☐	☐	☐	(neve)	☐ 1-2	☐ 3-4	☐ 5-6	☐ 7+

Prøv så godt du kan å gi et «gjennomsnitt» av matvanene dine.
Ha det siste året i tankene når du fyller ut.

18. Kosttilskudd (ts = teskje, bs = barneskje)

	Aldri/ sjelden	Gang pr. uke 1	2-3	4-5	6-7	Mengde pr. gang			
Tran	☐	☐	☐	☐	☐	1 ts ☐	1 bs ☐	1 ss ☐	
Trankapsler	☐	☐	☐	☐	☐	(kapsler) 1 ☐	2 ☐	3 ☐	4+ ☐
Fiskeoljekapsler, omega-3 tilskudd	☐	☐	☐	☐	☐	(kapsler) 1 ☐	2 ☐	3 ☐	4+ ☐
Seloljekapsler	☐	☐	☐	☐	☐	(kapsler) 1 ☐	2 ☐	3 ☐	4+ ☐

Multipreparater	Aldri/ sjelden	Gang pr. uke 1	2-3	4-5	6-7	Mengde pr. gang 1	2	3	4+
Sana-sol	☐	☐	☐	☐	☐	(bs) ☐	☐	☐	☐
Biovit	☐	☐	☐	☐	☐	(bs) ☐	☐	☐	☐
Mulitvitamin og mineral (eks. Vitamineral)	☐	☐	☐	☐	☐	(tablett) ☐	☐	☐	☐
Multivitaminer (uten mineraler)	☐	☐	☐	☐	☐	(tablett) ☐	☐	☐	☐

Jernpreparater	Aldri/ sjelden	Gang pr. uke 1	2-3	4-5	6-7	Mengde pr. gang 1	2	3	4+
Duroferon Duretter, Ferromax	☐	☐	☐	☐	☐	(tablett) ☐	☐	☐	☐
Hemofer, hemjern	☐	☐	☐	☐	☐	(tablett) ☐	☐	☐	☐
Amino Jern	☐	☐	☐	☐	☐	(tablett) ☐	☐	☐	☐
Jernmikstur (eks. Floradix)	☐	☐	☐	☐	☐	(bs) ☐	☐	☐	☐

Annet	Aldri/ sjelden	Gang pr. uke 1	2-3	4-5	6-7	Mengde pr. gang 1	2	3	4+
B-vitaminer (flere b-vitaminer i samme tablett)	☐	☐	☐	☐	☐	(tablett) ☐	☐	☐	☐
C-vitamin (60 mg/tablett)	☐	☐	☐	☐	☐	(tablett) ☐	☐	☐	☐
D-vitamin (10 µg/tablett)	☐	☐	☐	☐	☐	(tablett) ☐	☐	☐	☐
E-vitamin (30 mg/tablett)	☐	☐	☐	☐	☐	(tablett) ☐	☐	☐	☐
Folat (folsyre) (200 µg/tablett)	☐	☐	☐	☐	☐	(tablett) ☐	☐	☐	☐

Annet (inkludert helsekostpreparater). Noter navn på preparatet, hvor ofte og hvor mye du tar pr. gang.

Prøv så godt du kan å gi et «gjennomsnitt» av matvanene dine.
Ha det siste året i tankene når du fyller ut.

19. Måltider

Hvor ofte pleier du å spise følgende måltider i løpet av en uke? (Sett ett kryss for hvert måltid)

	Aldri/ sjelden	1 gang i uken	2 ganger i uken	3 ganger i uken	4 ganger i uken	5 ganger i uken	6 ganger i uken	Hver dag
Frokost	☐	☐	☐	☐	☐	☐	☐	☐
Formiddagsmat/lunsj	☐	☐	☐	☐	☐	☐	☐	☐
Middag	☐	☐	☐	☐	☐	☐	☐	☐
Kveldsmat	☐	☐	☐	☐	☐	☐	☐	☐

Hvor mange ganger i løpet av dagen pleier du å spise et eller annet utenom hovedmåltidene? (eks. godteri, frukt, brødskive)

Sjelden	1 gang om dagen	2 ganger om dagen	3 ganger om dagen	4 ganger om dagen	Mer enn 4 ganger om dagen
☐	☐	☐	☐	☐	☐

20. Eventuelle andre matvarer

Bruker du regelmessig matvarer, drikker eller andre produkter som ikke er nevnt i spørreskjemaet? Skriv ned dette så detaljert som mulig. Skriv også hvor ofte du spiser/drikker dette (ganger per måned eller uke) og hvor mye du spiser av dette per gang.

BRUK BLOKKBOKSTAVER

Tromsø-
undersøkelsen

Ditt bidrag teller!

Takk for at du stiller opp og bidrar til viktig forskning.

Returadresse:

Institutt for samfunnsmedisin.
Det helsevitenskapelige fakultet, UiT Norges arktiske universitet.
9037 Tromsø

Appendix 7

Study approval from the Regional Committees for Medical and Health Research Ethics (REK)

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK sør-øst C	Claus Henning Thorsen	22845515	28.11.2019	43798
			Deres referanse:	

Monica Hauger Carlsen

43798 Kosthold og kostholdsfaktorer som prediktorer for skrøpelighet blant eldre

Forskningsansvarlig: Universitetet i Oslo

Søker: Monica Hauger Carlsen

Søkers beskrivelse av formål:

Andelen eldre over 65 år øker raskt både i Norge og EU. Sunn aldring er fravær av sykdom og opprettholdelse av funksjonell evne. Mange eldre opplever imidlertid ikke sunn aldring. Skrøpelighet er et flerdimensjonalt geriatrisk syndrom kjennetegnet ved tap av fysisk funksjon, utilsiktet vekttap, lav aktivitet, tretthet, svekket kognitiv funksjon og økt risiko for uønskede helseutfall ved stress eller traume. Et usunt kosthold kan påvirke aldringsprosessen og utviklingen av skrøpelighet negativt. Formålet med prosjektet er å undersøke i hvilken grad kosthold og kostholdsendringer over tid påvirker risikoen for å utvikle skrøpelighet hos eldre personer. Vi vil bruke data fra gjentatte målinger av kosthold og helseutfall i Tromsøundersøkelsen. Resultatene fra prosjektet vil muliggjøre utvikling av kostråd og anbefalinger for å forbedre kosthold, helse og livskvalitet hos eldre, som på sikt igjen vil kunne bidra til reduserte kostnader for samfunnet.

REKs vurdering

Dette er en kvantitativ epidemiologisk observasjonsstudie basert på allerede innsamlede data om kosthold og helseutfall i Tromsøundersøkelsen. Man vil undersøke i hvilken grad kost og kostendringer påvirker risikoen for å utvikle skrøpelighet hos eldre, og man ønsker derfor å se på kostholdsregistreringer i et longitudinelt perspektiv.

Søker påpeker at prosjektet, i lys av det statlige fokuset på aldring og ernæring, jf. den godkjente statlige reformen « Leve hele livet», er svært relevant og vil gi ny kunnskap om forholdet mellom kosthold og skrøpelighet i et langsiktig perspektiv.

Studiepopulasjonen består av deltakere i Tromsøstudie 2-7, til sammen ca. 44.000 personer.

Komiteen har merket seg følgende fra søknad vedrørende samtykke «*Samtykke har allerede blitt innhentet for deltakere i Tromsø 4-7. Gjenlevende møtt før Tromsø 4 og ikke møtt senere (ikke gitt samtykke senere) er kontaktet for mulighet for reservasjon*.»

Videre angis under punktet **Ethical perspectives** i protokollen: "*All necessary ethical permissions and informed consents are already in place for the Tromsø Study."*

I henhold til søknadens punkt 6.14 ivaretas deltakernes rettigheter gjennom Tromsøundersøkelsens behandling og utlevering av data.

Komiteen har ingen forskningsetiske innvendinger til studiens gjennomføring. Prosjektstart er angitt til 02.09.2019, men komiteen forutsetter at studiespesifikke prosedyrer ikke er igangsatt.

Vedtak

Godkjent

Komiteen har gjort en helhetlig forskningsetisk vurdering av alle prosjektets sider. Prosjektet godkjennes med hjemmel i helseforskningsloven § 10.

Komiteen gjør samtidig oppmerksom på at etter ny personopplysningslov må det også foreligge et behandlingsgrunnlag etter personvernforordningen. Det må forankres i egen institusjon.

Tillatelsen er gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknaden og protokollen, og de bestemmelser som følger av helseforskningsloven med forskrifter.

Tillatelsen gjelder til 31.08.2023. Av dokumentasjons- og oppfølgingshensyn skal opplysningene likevel bevares inntil 31.08.2028. Opplysningene skal lagres avidentifisert, dvs. atskilt i en nøkkel-og en opplysningsfil. Opplysningene skal deretter slettes eller anonymiseres, senest innen et halvt år fra denne dato.

Komiteens avgjørelse var enstemmig.

Britt Ingjerd Nesheim
professor dr. med.
leder REK sør-øst C

Claus Henning Thorsen
Seniorrådgiver

Dokumentet er elektronisk signert

Kopi av vedtak: Universitetet i Oslo