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Body mass index and waist circumference as predictors of pre-frailty/frailty among older adults: A prospective cohort study

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Abstract

Objective: To explore the impact of body mass index (BMI) and waist circumference (WC), separately and concurrently, on the risk of pre-frailty/frailty among older adults during 21 years of follow-up.

Design: Prospective cohort study.

Setting: Population-based study among community-dwelling older adults in Tromsø municipality, Norway.

Participants: 2340 women and 2169 men aged ≥45 years attending the Tromsø Study in 1994–1995 (Tromsø4) and 2015–2016 (Tromsø7), with additional BMI and WC measurements in 2001 (Tromsø5) and 2007–2008 (Tromsø6).

Primary outcome measures: Modified Fried's frailty criteria were used to assess frailty status in Tromsø7. BMI and WC trajectories were identified using group-based trajectory modelling. Multivariable logistic regression was used to assess the effect of BMI and WC on frailty status over time.

Results: Participants with baseline obesity (adjusted odds ratio [OR] 2.41, 95% confidence interval [CI] 1.93–3.02) or overweight (OR 1.19, 95% CI 1.02–1.39) were more likely to be pre-frail/frail than those with normal BMI. Participants with high (OR 2.14, 95% CI 1.59–2.87) or moderately high (OR 1.57, 95% CI 1.21–2.03) baseline WC were more likely to be pre-frail/frail than those with normal WC. Those at baseline with normal BMI but moderately high/high WC or overweight with normal WC had no significantly increased odds for pre-frailty/frailty. However, those with both obesity and moderately high/high WC had increased odds of pre-frailty/frailty. Higher odds of pre-frailty/frailty was observed among those in "overweight to obesity" or "increasing obesity" trajectories than those with stable normal BMI. Compared with participants in a stable normal WC trajectory, those with high WC throughout follow-up were more likely to be pre-frail/frail.

Conclusion: Both general and abdominal obesity, especially over time during adulthood, is associated with an increased risk of pre-frailty/frailty. Thus maintaining normal BMI and WC throughout the life course is important.

Strengths and limitations of this study:

1. This study is a prospective cohort study with a follow-up period of 21 years.
2. This study takes into account changes in body mass index (BMI) and waist circumference (WC) through the follow-up period using repeated measures.
3. Frailty status was defined using a modified version of Fried's physical frailty criteria.
4. Frailty and pre-frailty were combined as one outcome.
5. Frailty could not be assessed at baseline.

Background

Frailty is a dynamic multifactorial geriatric syndrome characterised by physiological deterioration, increased vulnerability and decreased resilience toward external stressors.[1,2] Frailty is associated with an increased risk of adverse events such as falls, disability, hospitalisation, reduced quality of life, and mortality.[1,2] It is preceded by pre-frailty, a multi-dimensional, transitional risk state.[3,4] Fried's frailty phenotype identifies pre-frailty as the presence of one or two and frailty as three or more of the five criteria: unintentional weight loss, self-reported exhaustion, weakness, slow walking speed, and low physical activity.[5]

Rapid population ageing has become a global phenomenon.[6] Ageing is typically associated with changes in body composition, such as decreased muscle mass and redistribution of total and regional fat.[7–9] Underweight older adults with minimal reserve capacity are at risk of adverse health outcomes[5,10], and unintentional weight loss is commonly acknowledged as a significant frailty indicator.[5] However, a growing body of evidence also suggests a positive association between obesity among older adults and the risk of frailty.[9,11–15] Obesity aggravates the age-related decline in muscle strength, aerobic capacity, and physical functionality, thus worsening health and well-being.[9,10,13,16,17] It is also closely associated with metabolic disorders, inflammaging and oxidative stress, all of which have been suggested to contribute to the risk of frailty.[13,18]

Body mass index (BMI) and waist circumference (WC) are simple and widely used anthropometric measures. BMI indicates general obesity, while WC indicates abdominal obesity. When used together, both measures could effectively assess obesity-related risks at the population level. [19–21] Some studies have detected a U-shaped association between BMI and frailty.[12,14,22] Midlife overweight and obesity, defined by BMI, have been associated with the risk of pre-frailty and frailty in older age.[23,24] Similarly, a positive association between high WC and frailty among older adults has been observed in some studies.[8,15,25–27] These findings are even more relevant in the present context, where obesity prevalence is increasing across all age groups, posing a global public health challenge.[28]

Though the evidence is expanding, there have been limited longitudinal studies exploring and comparing the relationship of BMI and WC with the risk of developing pre-frailty and frailty over a long follow-up period.[27] Few have explored changes in BMI[29,30] and its association with frailty, while studies that consider changes in WC in association with the development of frailty seem to be lacking. Therefore, the present study aimed to investigate the impact of BMI and WC, separately and concurrently, on the risk of pre-frailty/frailty after 21 years of follow-up. Additionally, the present study assessed changes in BMI and WC through the follow-up period and their effect on pre-frailty/frailty.

Methods

The Tromsø study

The Tromsø Study is an ongoing population-based study in the Tromsø municipality, Norway, consisting of seven surveys: Tromsø1 (1974), Tromsø2 (1979–1980), Tromsø3 (1986–1987), Tromsø4 (1994–1995), Tromsø5 (2001), Tromsø6 (2007–2008), and Tromsø7 (2015–2016). More than 45,000 women and men have participated in at least one of the surveys.[31] The earlier surveys (Tromsø1-Tromsø3) did not include WC measurements. Therefore, the present study uses data from Tromsø4 (baseline) to Tromsø7 (follow-up). Data collection in Tromsø4–Tromsø7 included Visit 1 (questionnaires, biological sampling, clinical examinations) of the total sample and Visit 2 (additional clinical examinations) of a predefined subsample.[31]

Study sample

Tromsø4 included 27,158 participants aged 25–97 years (attendance 77%), Tromsø5, 8,130 participants aged 30–89 years (attendance 79%), Tromsø6, 12,984 participants aged 30–87 years (attendance 66%), and Tromsø7, 21,083 participants aged 40–99 years (attendance 65%).[31]

The present study included Tromsø4 participants aged ≥45 years with valid information on BMI who also attended Tromsø7, i.e., 21 years of follow-up (n = 4,809). Participants with missing information on three or more frailty indicators in Tromsø7 were excluded (Figure 1). Our primary analytical sample had 4,509 participants. Out of these, 1,534 participants had information on WC at Tromsø4 (only available among Visit 2 participants), and 1,391 had repeated measurements on both BMI and WC between Tromsø4 and Tromsø7.

Exposure

Bodyweight in kilograms and height in metres were measured wearing light clothes and no footwear. WC was measured using tape to the nearest centimetre at the umbilical level. All measurements were performed by trained personnel. BMI was calculated as the weight divided by the square of the height (kg/m^2) and categorised as underweight (<18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), and obesity (≥30.0 kg/m^2) according to the World Health Organization (WHO) criteria.[32] WC was categorised as normal (men ≤94 cm, women ≤80 cm), moderately high (men 95–102 cm, women 81–88 cm), and high (men>102 cm, women >88 cm) according to WHO.[33]

Frailty assessment

A modified version of Fried et al.'s frailty phenotype[5] was used to operationalise frailty in Tromsø7. Frailty was not operationalised at baseline as complete information on frailty indicators was unavailable. Five indicators were assessed at follow-up (Supplementary Table 1):

1. Unintentional weight loss: Self-reported involuntary weight loss during the last six months.[34]
2. Exhaustion: Response "pretty much" or "very much" to the question: "During the last week, have you experienced that everything is a struggle?" from the Hopkins' Symptom Checklist-10.[35]
3. Walking speed: Short Physical Performance Battery test, [36,37] where the fastest time out of two walks was selected and converted to seconds per 15 feet from seconds per 4 meters. Sex- and height-adjusted cut-offs, according to Fried et al.,[5] were used to identify participants with a low walking speed.
4. Weakness: Grip strength was measured using a newly calibrated Jamar+ Digital Dynamometer (Patterson Medical, Warrenville, IL, USA) following the Southampton protocol procedures.[38] Sex- and BMI-specific cut-offs, as suggested by Fried et al.,[5] were used to identify participants with low grip strength.
5. Low physical activity: Response "Reading, watching TV/screen or other sedentary activity" to the question: "Describe your exercise and physical exertion in leisure time over the last year" from the Saltin–Grimby Physical Activity Level Scale for leisure-time physical activity.[39]

Participants were categorised as robust (0), pre-frail (1-2) and frail (≥3) based on the number of frailty indicators present. The number of participants with frailty was low in the present study (<1.1%); hence pre-frail and frail individuals were combined to form a common outcome, i.e. pre-frail/frail (frailty score ≥1).

Covariates

The potential covariates in this study were selected based on the existing knowledge and literature on frailty status. Sociodemographic characteristics included age, sex, educational level [primary/partly secondary education (up to 10 years of schooling), upper secondary education (minimum of 3 years), college/university short (<4 years), and college/university long (≥4 years)], and marital/cohabitation status (married/cohabiting or single/not cohabiting with a partner). Self-reported smoking status was categorised as current, former, or never smoker. Self-reported alcohol intake level was categorised as never-drinker, infrequent drinker (<2–4 times/month), and frequent drinker (>2–3 times/week). Comorbidity was defined using Charlson's comorbidity index[40] without weighting of the diseases. It was categorised as "no comorbidity" and "comorbidity" based on the self-reported presence of coronary heart disease (angina pectoris/myocardial infarction), stroke, diabetes, cancer, pulmonary disease (asthma/chronic bronchitis/emphysema), and peptic ulcer. Social support was categorised as self-reported "not enough good friends" or "enough good friends." Self-perceived health status was categorised as "poor" or "good." Baseline physical activity level was categorised as no/low physical activity (0 hours/week spent in hard physical activity or ≤2 hours/week spent in light physical activity) and high physical activity (≥1 hour/week in hard physical activity or ≥3 hours/week in light physical activity).

Statistical analysis

The sociodemographic and lifestyle factors at baseline across robust and pre-frail/frail groups were described using mean and standard deviation for continuous variables and proportion and count for categorical variables. The differences between the two groups were tested using the student's *t*-test for continuous variables and the chi-square test for categorical variables.

Multivariable logistic regression analysis was used to assess the effect of BMI and WC on pre-frailty/frailty at follow-up. Five different longitudinal associations were assessed: baseline BMI and pre-frailty/frailty; baseline WC and pre-frailty/frailty; joint BMI and WC profile at baseline and pre-frailty/frailty; BMI trajectories and pre-frailty/frailty; WC trajectories and pre-frailty/frailty. The models were minimally adjusted for age and sex (Model 1) and further adjusted for educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level at baseline (Model 2). The adjustment variables were selected using a stepwise backward regression procedure. No significant collinearity or interaction was detected between covariates in the model.

Group-based trajectory modelling (GBTM) was conducted among 1,391 participants to assess changes in the BMI and WC throughout the 21-year follow-up period, with four repeated measurements on both BMI and WC, taken every 6-7 years at Tromsø4, Tromsø5, Tromsø6 and Tromsø7. GBTM, also known as latent class growth analysis, is a semi-parametric technique that identifies distinct subgroups of individuals following a similar pattern of change over time on a given variable, using finite mixtures of defined probability distributions.[41] Different models with varying numbers of trajectory groups, varying functional forms and orders were compared. The most appropriate model was selected based on the Bayesian Information Criterion[42] and then introduced into longitudinal multivariable logistic regression models. The distinct BMI and WC trajectories were named based on their observed pattern. The WC trajectories were sex-stratified due to varying cut-off levels for men and women.

A new variable with five distinct strata (normal BMI and normal WC; normal BMI and moderately high/high WC; overweight and low WC; overweight and moderately high/high WC; obesity and moderately high/high WC) was formed by combining different categories of BMI and WC. They were then introduced into the multivariable models to assess the concurrent effects of BMI and WC on frailty status. While

forming the new joint variable, the underweight group was removed because of low prevalence (<1%), and moderately high and high WC groups were combined because of their low sample size when stratified.

Additional supplementary analyses were carried out. The primary longitudinal analyses were repeated among the subgroup of participants with non-missing information on all five frailty indicators (*n* = 2,864), and cross-sectional analyses were performed to assess the association between BMI and WC level and frailty status at Tromsø7.

All the statistical analyses were conducted using STATA 16.[43] Statistical significance was set at $P < 0.05$. The results are expressed as adjusted odds ratios (ORs) with 95% confidence intervals (CIs).

Patient and public involvement

Patients and the public were not involved in this research's design, conduct, reporting, or dissemination plans.

Results

Study population

The mean age at baseline was 51.6 years, and the participants were followed up for 21 years. 28.4% of the participants were pre-frail, 1.1% were frail, and 70.5% were robust at follow-up (Table 1). In total, 50.6% of the robust group and 55.0% of the pre-frail/frail group were women. Most robust and pre-frail/frail participants were either married or cohabiting (84.3% and 80.3%) and reported having enough good friends (83.1% and 80.5%) at baseline. All the baseline characteristics, except comorbidity, were significantly different in the robust and the pre-frail/frail groups (Table 1).

When assessed at follow-up, all the sociodemographic, lifestyle and disease-related factors were significantly associated with pre-frailty/frailty (Supplementary Table 2). When the baseline characteristics of the eligible participants lost to follow-up (*n* = 8,649) were compared with those of the attendees, they were found to be older (mean age 63.2 years) with a less healthy lifestyle and higher comorbidities (Supplementary Table 3).

BMI and WC

At baseline, the proportion of individuals with underweight was low (<1%) (Table 2). The proportion of individuals with normal BMI was higher among the robust group than the pre-frail/frail group (47.6% versus 39.3%), whereas the proportion of individuals with obesity was higher among the pre-frail/frail group

(17.1% versus 8.4%). The robust group had a higher proportion of individuals with normal WC than the pre-frail/frail group (51.5% versus 37.3%), whereas the pre-frail/frail group had a higher proportion of individuals with high WC (27.7% versus 17.4%). A similar distribution of different BMI and WC categories across robust and pre-frail/frail groups was observed at follow-up (Supplementary Table 2). Both robust and pre-frail/frail groups at follow-up had an increased proportion of individuals with obesity and high WC compared with baseline (Table 2; Supplementary Table 2).

Table 1 Baseline characteristics of participants by frailty status at follow-up: The Tromsø Study 1994–2016

	Frailty status		
	Robust (% (*n*)) 70.5 (3,179)	**Pre-frail/frail (% (*n*)) 29.5 (1,330)**	***P* value**
Age in years, mean (SD)	51.1 (5.1)	52.8 (5.9)	<0.05[a]
Women	50.6 (1,608)	55.0 (732)	<0.05
Smoking status			
Current smokers	27.0 (858)	33.7 (448)	
Former smokers	36.1 (1,149)	34.0 (452)	<0.05
Never	36.9 (1,172)	32.3 (430)	
High physical activity level	69.5 (2,210)	56.9 (756)	<0.05
Married or cohabiting	84.3 (2,679)	80.3 (1,068)	<0.05
Self-perceived health – good	75.4 (2,394)	61.5 (818)	<0.05
Social support – enough good friends	83.1 (2,404)	80.5 (976)	<0.05
Educational level			
Primary/Partly secondary	32.8 (1,041)	42.4 (562)	
Upper secondary	34.3 (1,085)	34.2 (453)	<0.05
College/University short	16.5 (524)	12.8 (169)	
College/University long	16.4 (520)	10.6 (141)	
Alcohol intake			
Never/Abstaining	9.0 (286)	11.9 (158)	
Infrequent drinker	76.2 (2,419)	76.6 (1,015)	<0.05
Frequent drinker	14.8 (468)	11.5 (152)	
Prevalent diseases			
Pulmonary disease[b]	8.6 (272)	9.5 (126)	>0.05
Coronary heart disease[c]	2.3 (73)	4.5 (59)	<0.05
Diabetes	0.4 (12)	0.6 (8)	0.05
Cancer	2.8 (79)	3.5 (42)	>0.05
Stroke	0.6 (19)	0.8 (11)	>0.05
Peptic ulcer	7.0 (197)	8.9 (105)	<0.05
Comorbidity	1.9 (59)	2.7 (36)	>0.05

Values are percentages (numbers); *P* value: χ^2 test for categorical variables; *P* value: [a]Student's t-test; [b]including asthma/chronic bronchitis/emphysema; [c]including angina pectoris/myocardial infarction.

When BMI and WC level was assessed jointly at baseline (Table 3), the robust group had a higher proportion of individuals with both BMI and WC in the normal range than the pre-frail/frail group (36.1% versus 29.1%). The proportion of individuals with both obesity and moderately high/ high WC was higher among the pre-frail/frail group (16.9% versus 7.4%).

The GBTM resulted in four distinct trajectories of BMI (n = 1391): stable normal BMI (25.8%), stable overweight (44.8%), overweight to obesity (23.9%), and increasing obesity (5.5%) (Supplementary Figure 1). The increasing obesity trajectory included the individuals with BMI ≥30 kg/m² at baseline, which kept increasing to a higher obesity level, i.e., BMI ≥35 kg/m². Four distinct WC trajectories were identified for both women (n = 660) and men (n = 731) (Supplementary Figure 2). The WC trajectories for women were: stable normal WC (23.3%), moderately high to high WC (45.8%), gradually increasing high WC (26.6%), and steeply increasing high WC (4.3%). The WC trajectories for men were: stable normal WC (21.0%), stable moderately high WC (39.9%), moderately high to high WC (30.6%), and increasing high WC (8.5%).

BMI, WC, and pre-frailty/frailty

Individuals who had obesity (OR 2.41, 95% CI 1.93–3.02) or overweight (OR 1.19, 95% CI 1.02–1.39) at baseline had significantly higher odds of becoming pre-frail/frail at follow-up compared with individuals with normal BMI (Model 2, Table 2). No statistically significant association was detected between underweight BMI and the odds of pre-frailty/frailty; however, the number of underweight individuals was insufficient to reach any conclusion. Participants with moderately high WC (OR 1.57, 95% CI 1.21–2.03) or high WC (OR 2.16, 95% CI 1.59–2.87) at baseline had higher odds of becoming pre-frail/frail at follow-up compared to individuals with a normal WC (Model 2, Table 2).

When this analysis was repeated among participants with complete information on all five frailty criteria (n = 2,864; Supplementary Table 4), it generated similar results, except for participants with overweight BMI (OR 1.18, 95% CI 0.97–1.43).

The supplementary cross-sectional analysis (Supplementary Table 5) indicated a significant association between obesity and pre-frailty/frailty among older adults (OR 1.88, 95% CI 1.54–2.30), whereas no association was detected between overweight and pre-frailty/frailty. As for WC, only high WC was associated with increased odds of pre-frailty/frailty (OR 1.45, 95% CI 1.20–1.76) in the cross-sectional analysis.

Table 2 Longitudinal association between BMI and WC, and pre-frailty/frailty: The Tromsø Study 1994–2016

	Frailty status			
	Robust (% (*n*))	**Pre-frail/frail (% (*n*))**	**Model 1 OR (95% CI)**	**Model 2 OR (95% CI)**
	70.5 (3179)	29.5 (1330)		
BMI, kg/m²				
Underweight	0.3 (11)	0.7 (9)	2.15 (0.88–5.29)	1.32 (0.49–3.54)
Normal	47.6 (1,513)	39.3 (522)	Ref.	Ref.
Overweight	43.7 (1,388)	43.0 (572)	1.18 (1.02–1.36)	1.19 (1.02–1.39)
Obesity	8.4 (267)	17.0 (227)	2.42 (1.98–2.98)	2.41 (1.93–3.02)
WC, cm	*n* = 952	*n* = 582		

Normal	51.5 (490)	37.3 (217)	Ref.	Ref.
Moderately high	31.1 (296)	35.0 (204)	1.54 (1.21–1.96)*	1.57 (1.21–2.03)*
High	17.4 (166)	27.7 (161)	2.16 (1.65–2.83)*	2.14 (1.59–2.87)*

Model 1: adjusted for age and sex (*excluding sex) at baseline.
Model 2: adjusted for age, sex, educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level (*excluding sex) at baseline.
BMI, body mass index; CI, confidence interval; OR: odds ratio; WC, waist circumference.

BMI categories
Underweight: <18.5 kg/m^2
Normal: 18.5–24.9 kg/m^2
Overweight: 25.0–29.9 kg/m^2
Obesity: ≥30 kg/m^2

WC categories
Normal: men ≤94 cm; women ≤80 cm
Moderately high: men 95–102 cm; women 81–88 cm
High: men >102 cm; women >88 cm

The longitudinal model that included joint BMI and WC profile at baseline showed that participants who had overweight with moderately high/high WC (OR 1.48, 95% CI 1.11–1.98) or participants who had obesity with moderately high/high WC (OR 3.11, 95% CI 2.07–4.70) had higher odds of being pre-frail/frail compared with participants with normal BMI and normal WC (Model 2, Table 3). No significant association with pre-frailty/frailty was detected among participants who had normal BMI with moderately high/high WC or overweight with normal WC at baseline.

Table 3 Association between combined BMI and WC profiles, and pre-frailty/frailty: The Tromsø Study 1994–2016

	Frailty status			
Longitudinal	**Robust (% (*n*))**	**Pre-frail/frail (% (*n*))**	**Model 1 OR (95% CI)**	**Model 2 OR (95% CI)**
BMI and WC profile, baseline	62.8 (870)	37.2 (515)		
Normal BMI and normal WC	36.1 (314)	29.1 (150)	Ref.	Ref.
Normal BMI and moderately high/high WC	8.4 (73)	8.0 (41)	1.13 (0.73–1.74)	1.01 (0.63–1.61)
Overweight and normal WC	15.9 (139)	9.5 (49)	0.74 (0.50–1.08)	0.79 (0.53–1.19)
Overweight and moderately high/high WC	32.2 (280)	36.5 (188)	1.40 (1.07–1.84)	1.48 (1.11–1.98)
Obesity and moderately high/high WC	7.4 (64)	16.9 (87)	2.86 (1.96–4.18)	3.11 (2.07–4.70)

Model 1: adjusted for age at baseline.
Model 2: adjusted for age, educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level at baseline.
BMI, body mass index; CI, confidence interval; OR: odds ratio; WC, waist circumference.

The model with BMI trajectories (Model 2, Table 4) indicated higher odds of pre-frailty/frailty among participants in the overweight to obesity trajectory (OR 1.67, 95% CI 1.19–2.35) or those in the constantly increasing obesity trajectory (OR 3.12, 95% CI 1.80–5.41) compared with those in the stable normal BMI trajectory. In contrast, there was no significant association in the stable overweight category. The model with WC trajectories (Model 2, Table 4) showed that women in the gradually increasing high WC trajectory (OR 2.17, 95% CI 1.32–3.59) or the steeply increasing high WC trajectory (OR 4.09, 95% CI 1.54–10.90) had higher odds of being pre-frail/frail compared with women in the normal WC trajectory. Similarly, men in the increasing high WC trajectory (OR 3.36, 95% CI 1.71–6.59) had higher odds of pre-frailty/frailty compared with men in the normal WC trajectory.

Table 4 Association between BMI and WC trajectories and pre-frailty/frailty: The Tromsø study 1994–2016

	Frailty status		Model 1	Model 2
	Robust (% (*n*))	Pre-frail/frail (% (*n*))	OR (95% CI)	OR (95% CI)
	62.8 (874)	37.2 (517)		
BMI trajectories				
Stable normal BMI	27.8 (243)	22.4 (116)	Ref.	Ref.
Stable overweight	46.6 (407)	42.4 (219)	1.20 (0.91–1.59)	1.21 (0.90–1.62)
Overweight to obese	21.8 (191)	26.5 (137)	1.62 (1.18–2.22)	1.67 (1.19–2.35)
Increasing obesity	3.8 (33)	8.7 (45)	3.07 (1.85–5.09)	3.12 (1.80–5.41)
	59.4 (392)	40.6 (268)		
WC trajectories (women)				
Stable normal WC	26.3 (103)	17.5 (47)	Ref.	Ref.
Moderately high to high WC	49.7 (195)	42.5 (114)	1.27 (0.84–1.94)*	1.30 (0.83–2.05)*
Gradually increasing high WC	20.9 (82)	33.6 (90)	2.34 (1.47–3.70)*	2.17 (1.32–3.59)*
Steeply increasing high WC	3.1 (13)	6.3 (17)	3.04 (1.34–6.90)*	4.09 (1.54–10.90)*
	65.9 (482)	34.1 (249)		
WC trajectories (men)				
Stable normal WC	22.4 (108)	18.1 (45)	Ref.	Ref.
Stable moderately high WC	41.1 (198)	38.5 (96)	1.18 (0.77–1.80)*	1.12 (0.72–1.76)*
Moderately high to high WC	31.5 (152)	28.9 (72)	1.18 (0.75–1.85)*	1.12 (0.69–1.79)*
Increasing high WC	5.0 (24)	14.5 (36)	3.73 (1.99–6.97)*	3.36 (1.71–6.59)*

Model 1: adjusted for age and sex at baseline (*adjusted for age only).
Model 2: adjusted for age, sex, educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level (*excluding sex) at baseline.
BMI, body mass index; CI, confidence interval; OR: odds ratio; WC, waist circumference.

Discussion

The present study followed 4,509 community-dwelling participants from the population-based Tromsø Study from 1994 to 2016 to examine the association between general and abdominal obesity and the risk of frailty. This study suggests an increased likelihood of pre-frailty/frailty among those with overweight or obesity. Increased likelihood of pre-frailty/frailty was also observed among those with high or moderately high WC at baseline. When assessed jointly, participants with both obesity and moderately high/high WC at baseline had increased odds of being pre-frail/frail compared to those with BMI and WC in the normal range. Participants in the "overweight to obesity" or the "increasing obesity" trajectories had increased odds of pre-frailty/frailty compared with those in the stable normal BMI trajectory. Additionally, participants with a high WC at baseline, whose WC gradually or steeply increased throughout the follow-up period, had increased odds of being pre-frail/frail compared with those in a stable normal WC trajectory.

In line with our conclusions, the findings from two previous longitudinal studies with a similar follow-up period (26 and 22 years) reported a significant positive association between midlife overweight or obesity and the development of pre-frailty and frailty in later life. [23,24] A prospective study with a follow-up period of 3.5 years observed a significantly increased risk of frailty among underweight women and women with overweight and obesity.[22] No significant association between baseline underweight status and the risk of pre-frailty/frailty was detected in our study. However, the number of underweight individuals in our study was too low, resulting in a low statistical power to reach any conclusion. When repeating our primary longitudinal analysis among a subsample of participants using stricter exclusion criteria, i.e. non-missing information on all five markers of frailty, only participants with obesity at baseline had an increased likelihood of becoming pre-frail/frail at follow-up.

In terms of WC and frailty status, similar to our results, a positive association between higher WC and frailty among older adults was reported by a 3.5-year follow-up study from two prospective Spanish cohorts.[27] A positive association between high WC and frailty was observed in a few other studies;[8,15,25] however, they were cross-sectional and used slightly different cut-offs to categorise WC.

We identified BMI and WC trajectories to account for the dynamic change in the adiposity level that might occur during the life course. In line with our findings regarding BMI trajectories, comparable trajectories and observations about a higher risk of pre-frailty and frailty among those with increasing BMI were observed in a 26-year follow-up study.[30] A large study that followed adults aged ≥51 years for ten years reported a higher incidence of frailty among weight gain class, weight loss class, and consistent obesity class.[29] Literature on long-term changes in WC and its association with frailty seems lacking. Few epidemiological studies have explored the combined effect of BMI and WC on frailty among older adults. Two studies conducted among adults aged ≥65 years in Portugal[44] and ≥60 years in Spain[27] observed a positive association between frailty and adiposity only when the individuals had both a high WC and a high BMI. It aligns with our result to a certain extent, as we observed an increased likelihood of pre-frailty/frailty among individuals with both obesity and moderately high/high WC at baseline. We also observed higher odds of pre-frailty/frailty among those who had overweight with a moderately high/high WC at baseline. On the contrary, high WC was reported to be associated with frailty regardless of their BMI categories by two cross-sectional studies conducted among community-dwelling adults aged ≥65 years in China[25] and England,[14] indicating WC to be better linked with frailty. Of note, participants who had normal BMI with moderately high/high WC or those who had overweight with normal WC did not have significantly increased odds of pre-frailty/frailty in our study. This finding indicates the importance of considering both BMI and WC to identify the risk of frailty.

There are different mechanisms through which obesity might contribute to pre-frailty/frailty. Increased adiposity leads to increased secretion of pro-inflammatory adipokines, thus contributing to inflammation,[13,18] which is also associated with frailty among older adults.[45] Obesity leads to increased fat mass and increased lipid infiltration in muscle fibres resulting in reduced muscle strength and function.[13,46] When coupled with an age-related decline in muscle mass and strength, it causes "sarcopenic obesity", which is linked to an increased risk of frailty and disability.[18,47,48]

We used anthropometric measurements (BMI and WC) to define general and abdominal obesity as our primary exposures. BMI is often criticised for its inability to provide information on fat distribution,[20] while WC is criticised for its limitation in distinguishing between visceral and subcutaneous fat.[49] However, they are effective in assessing obesity-related risks at the population level.[19,20] A study among Tromsø7 participants aged ≥40 years found a strong correlation between BMI and visceral adipose tissue (VAT) mass and WC and VAT mass. It also concluded them to be a satisfactory substitute to identify cardiometabolic risk.[21] Further, they are simple to measure, easy to replicate, and widely used in routine health assessments, thus, helping identify individuals at risk of frailty to provide timely interventions.

The primary strength of this study is its prospective design with a long follow-up period of two decades. Both BMI and WC were measured objectively. The repeated measures allowed us to account for changes in BMI and WC through the follow-up period and gain a more comprehensive understanding of the long-term effects of these exposures on the risk of frailty. We used a slightly modified version of Fried et al.'s frailty phenotype definition,[5] one of the most commonly used definitions in frailty research.[50] Each frailty indicator we utilised has been validated in different research contexts.[34–36,39] The main limitation of our study is the selection bias resulting from differential loss to follow-up. Those lost to follow-up were comparatively older and had a higher proportion of general and abdominal obesity and other potential risk factors for frailty (Supplementary Table 3). This might have led to a lower prevalence of frailty in Tromsø7. However, given the 21 years follow-up period, most of the participants might have been lost to follow-up because of mortality at an older age. In total, 1.1% of the participants aged ≥66 years at Tromsø7 were frail, and 28.4% were pre-frail which is much lower than the pooled prevalence estimates provided by O'Caoimh et al.[51] This result aligns with the findings from a study where the grip strengths of Tromsø7 participants and Russian Know Your Heart study participants aged 40-69 years were compared. The average Norwegian participant had a mean grip strength comparable to a seven-year younger Russian counterpart [52]. This indicates that the nordic population might be comparatively healthier,[53] thus limiting the generalisability of our findings to other populations across the globe. Only a sub-sample of our study population had information on both BMI and WC, and an even lower number had repeated measurements available for both exposures. Therefore, the models including both BMI and WC might have low statistical power, particularly when considering the repeated measures. Information on frailty measures was not available at baseline. However, most participants were in their mid-life (median age 50) at baseline, lowering their likelihood of having frailty components. We adjusted for several confounding factors; however, the potential for residual confounding remains. We could not adjust for inflammatory markers, which is a limitation.

We combined pre-frailty and frailty as a single outcome because of the low frailty prevalence in this study. The pre-frail/frail population in this study is primarily pre-frail. It would have been informative to assess the risk of the pre-frailty and frailty separately. Nevertheless, understanding factors associated with pre-frailty is highly relevant because pre-frailty is gaining broader interest as an ideal opportunity for administering timely intervention to delay or reverse frailty and the associated adverse outcomes.[54] Of note, as our outcome pre-frailty/frailty is common, the OR estimates obtained might slightly overestimate the relative risk, and caution should be applied while interpreting it as a risk.

In the context where the population is rapidly ageing, and the obesity epidemic is rising, growing evidence recognises the subgroup of "fat and frail" older individuals in contrast to viewing frailty only as a wasting disorder.[11,14,24] In our study, individuals with both high BMI and high WC, i.e., general and abdominal obesity, especially for a long duration throughout their adulthood, were observed to have an increased likelihood of pre-frailty/frailty. It highlights the importance of routinely assessing and maintaining optimal BMI and WC throughout adulthood to lower the risk of frailty in older age.

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Competing Interest

None declared.

Ethical approval

The Tromsø Study was approved by the Regional Committee of Medical and Health Research Ethics (REK) North and the Norwegian Data Protection Authority. Approvals from REK (ref. 2021/234146) and the Norwegian Centre for Research Data (NSD) (ref. 364331) were obtained for this particular study.

Contributions

SU was responsible for conceptualisation, data acquisition, analysis, interpretation, writing original draft, review and editing; LFA was responsible for conceptualisation, funding acquisition, supervision, writing critical review and editing; LAH was responsible for data acquisition for the Tromsø Study, constant coordination, writing critical review and editing; AH was responsible for conceptualisation, funding acquisition, data acquisition, supervision, writing critical review and editing.

Data availability statement

Not available

Patient consent for publication

Not required

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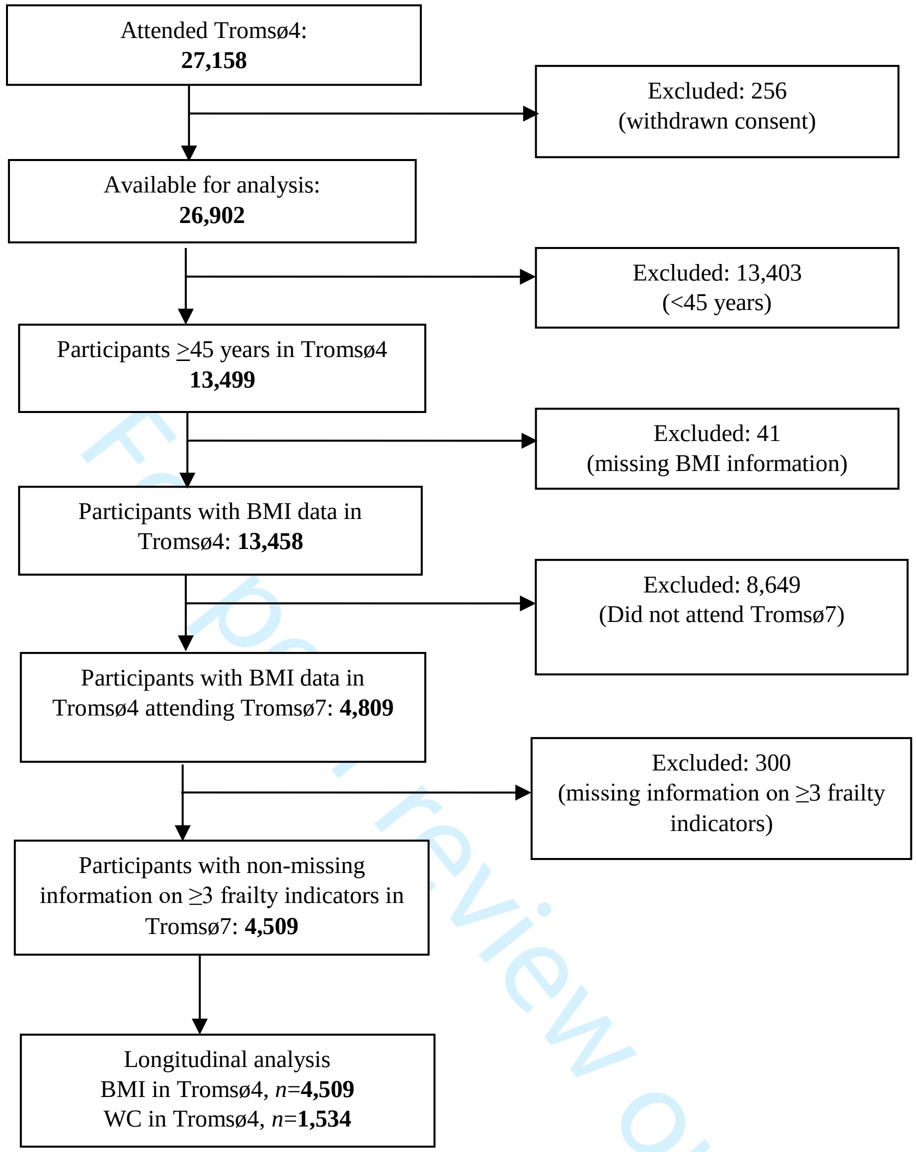


Figure 1 Flowchart displaying participants' inclusion and exclusion

SUPPLEMENTARY TABLES

Supplementary Table 1 Comparison between Fried et al.'s suggested criteria for frailty and modified frailty indicators used in this study

Frailty	Fried et al. (2001)	Current study
Exhaustion	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 day? 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 time (3–4 days) 3 = Most of the time **Exhausted: "A moderate amount of time (3–4 days)" or "Most of the time"**	Hopkins Symptom Checklist (HSCL-10): During the last week, have you experienced that everything is a struggle? 1 = No complaint 2 = Little complaint 3 = Pretty much 4 = Very much **Exhausted: "Pretty much" or "Very much"**
Physical activity	Minnesota Leisure Time Activity Questionnaire asking about walking, chores (moderately strenuous), mowing the lawn, raking, gardening, hiking, jogging, biking, exercise, cycling, dancing, aerobics, bowling, golf, singles, tennis, racquetball, calisthenics, swimming. The kcal/week expended was calculated using a standardized algorithm. Lowest 20% were identified, resulting in following cut-off for frailty: Men: <383 kcal of physical activity/week Women: <270 kcal of physical activity/week	Describe your exercise and physical exertion in leisure time over the last year (Saltin & Grimby's Scale). 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 shoveling, etc. at least 4 hours a week 4 = Participation in hard training or sports competitions, regularly several times a week **Low physical activity level: "Reading, watching TV/screen or other sedentary activity"**
Weight loss	In the last year, have you lost more than 10 pounds (4.5 kg) unintentionally (not due to dieting or exercise)? **Frail: "Yes"**	Have you involuntarily lost weight during the last 6 months? (Malnutrition Universal Screening Tool) 0 = No 1 = Yes **Frail: "Yes"**
Grip strength	Measured by Jamar dynamometer (kg) Maximal strength in dominant hand (3 trials) Stratified by sex and BMI quartiles. Lowest 20% were identified, resulting in the following cut-off for frailty: **Men** — **Cut-off for grip strength (kg) criterion for frailty** BMI ≤24 — ≤29 kg BMI 24.1–26 — ≤30 kg BMI 26.1–28 — ≤30 kg BMI >28 — ≤32 kg **Women** BMI ≤23 — ≤17 kg BMI 23.1–26 — ≤7.3 kg BMI 26.1–29 — ≤18 kg BMI >29 — ≤21 kg	Measured by Jamar dynamometer (kg) Strongest measurement from 3 trials in each hand Stratified by sex and BMI quartiles as per Fried's definition: **Men** — **Cut-off for grip strength (kg) criterion for frailty** BMI ≤24 — ≤29 kg BMI 24.1–26 — ≤30 kg BMI 26.1–28 — ≤30 kg BMI >28 — ≤32 kg **Women** BMI ≤23 — ≤17 kg BMI 23.1–26 — ≤17.3 kg BMI 26.1–29 — ≤18 kg BMI >29 — ≤21 kg

Frailty	Fried et al. (2001)	Current study
Walking speed	Time to walk (seconds) 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 frailty: **Men** — **Cut-off for walking speed criterion for frailty** Height ≤173 cm — ≥7 s Height >173 cm — ≥6 s **Women** Height ≤159 cm — ≥7 s Height >159 cm — ≥6 s	SPPB: Short Physical Performance Battery – walking test Fastest of two times (seconds) to walk 4 m stratified by sex and height according to Fried's gender-specific cut-off. Converted to feet from meters. **Men** — **Cut-off for walking speed criterion for frailty** Height ≤173 cm — ≥7 s Height >173 cm — ≥6 s **Women** Height ≤159 cm — ≥7 s Height >159 cm — ≥6 s
Frailty status	Frailty score: 0 = Robust 1–2 = Pre-frail ≥3 = Frail	Frailty score: 0 = Robust 1–2 = Pre-frail ≥3 = Frail Pre-frailty/frailty score: 0 = Robust ≥1 = Pre-frail/frail

Supplementary Table 2 Descriptive characteristics of participants at follow-up: The Tromsø Study 2015-2016

	Frailty status		
	Robust (% (n)) 70.5 (3,179)	**Pre-frail/ frail (% (n)) 29.5 (1,330)**	***P* value**
Age in years, mean (SD)	72.1 (5.1)	73.8 (5.9)	<0.05[a]
Women	50.6 (1608)	55.0 (732)	<0.05
Smoking status			
Current smokers	8.3 (262)	14.4 (188)	
Former smokers	53.2 (1,674)	50.8 (666)	<0.05
Never	38.4 (1,208)	34.8 (456)	
Married or cohabiting	71.0 (2,258)	64.6 (859)	<0.05
Self-perceived health – good	69.4 (2,178)	43.2 (566)	<0.05
Social support – enough good friends	87.4 (2,676)	82.0 (1,047)	<0.05
Educational level			
Primary/Partly secondary	39.1 (1,201)	50 (632)	
Upper secondary	26.6 (817)	26.2 (331)	<0.05
College/University short	16.3 (500)	12.2 (154)	
College/University long	18.1 (556)	11.6 (147)	
Alcohol intake			
Never/Abstaining	11.2 (352)	17.4 (229)	
Infrequent drinkers	58.6 (1,846)	61.0 (803)	< 0.05
Frequent drinkers	30.3 (954)	21.6 (284)	
Prevalent diseases			
Pulmonary disease[b]	14.6 (444)	19.9 (250)	<0.05
Coronary heart disease[c]	13.7 (415)	19.3 (241)	<0.05
Diabetes	7.3 (224)	14.8 (186)	<0.05
Cancer	15.6 (475)	19.3 (243)	<0.05
Stroke	5.1 (154)	8.1 (101)	<0.05
Peptic ulcer	–	–	<0.05
Comorbidity	89.8 (2,800)	82.4 (1,075)	<0.05
BMI categories			
Underweight	0.5 (17)	1.4 (18)	
Normal	30.0 (951)	24.5 (323)	<0.05
Overweight	49.4 (1,566)	41.4 (547)	
Obese	20.1 (639)	32.7 (432)	
WC categories			
Normal	22.6 (716)	17.1 (225)	
Moderately high	28.0 (888)	21.3 (281)	<0.05
High	49.4 (1,569)	61.6 (812)	

Values are percentage (number); P value: χ^2 test for categorical variables P value: [a]Student's t-test; [b]including asthma/chronic bronchitis/emphysema; [c]including angina pectoris/myocardial infarction. BMI, body mass index; WC, waist circumference.

BMI categories
Underweight: <18.5 kg/m^2
Normal: 18.5–24.9 kg/m^2
Overweight: 25.0–29.9 kg/m^2
Obesity: ≥30 kg/m^2

WC categories
Normal: men ≤94 cm; women ≤80 cm
Moderately high: men 95–102 cm; women 81–88 cm
High: men >102 cm; women >88 cm

Supplementary Table 3 Descriptive baseline characteristics of Tromsø4 participants who attended Tromsø7 versus those who did not: The Tromsø Study 1994–2016

	Frailty status		
	Not attended Tromsø7 n = 8,649 (% (n))	**Attended Tromsø7 n = 4,809 (% (n))**	***P* value**
Age in years, mean (SD)	63.2 (11.0)	52.0 (5.8)	<0.05[a]
Women	52.4 (4,533)	52.4 (2520)	>0.05
Smoking status			
Current smokers	33.7 (2,916)	29.4 (1,414)	
Former smokers	33.4 (2,886)	35.6 (1,714)	<0.05
Never	32.9 (2,847)	(34.9) 1,681	
Married or cohabiting	64.7 (5,568)	(82.7) 3,977	<0.05
Self-perceived health status – good	50.7 (4,378)	(70.3) 3,379	<0.05
Social support – enough good friends	83.0 (5,775)	(82.2) 3,590	>0.05
Educational level			
Primary/Partly secondary	57.2 (4,911)	(36.9) 1,768	
Upper secondary	27.5 (2,362)	(34.1) 1,633	<0.05
College/University short	8.1 (696)	(14.9) 716	
College/University long	7.2 (622)	(14.1) 678	
Alcohol intake			
Never/Abstaining	24.5 (2,108)	(10.2) 491	
Infrequent drinkers	66.8 (5,749)	(76.2) 3655	<0.05
Frequent drinkers	8.7 (744)	(13.5) 649	
Prevalent diseases			
Pulmonary disease[b]	16.2 (1,097)	(9.9) 430	<0.05
Coronary heart disease[c]	14.8 (1,281)	(3.1) 149	<0.05
Diabetes	4.3 (374)	(0.5) 25	<0.05
Cancer	7.7 (517)	(3.1) 132	<0.05
Stroke	3.7 (318)	(0.7) 33	<0.05
Ulcer	14.1 (908)	(7.8) 333	<0.05
Comorbidity	9.9 (858)	(2.3) 36	<0.05
BMI categories			
Underweight	1.7 (149)	0.5 (22)	
Normal	40.0 (3,463)	44.9 (2,169)	<0.05
Overweight	42.3 (3,659)	43.5 (2,094)	
Obesity	15.9 (1,378)	11.1 (533)	
WC categories			
Normal	39.0 (1,784)	45 (765)	
Moderately high	29.7 (1,356)	32.6 (554)	<0.05
High	31.3 (1,434)	22.4 (381)	

Values are percentage (number); P value: χ^2 test for categorical variables P value: [a]Student's t-test; [b]including asthma/chronic bronchitis/emphysema; [c]including angina pectoris/myocardial infarction. BMI, body mass index; WC, waist circumference.

BMI categories
Underweight: <18.5 kg/m^2
Normal: 18.5–24.9 kg/m^2
Overweight: 25.0–29.9 kg/m^2
Obesity: ≥30 kg/m^2

WC categories
Normal: men ≤94 cm; women ≤80 cm
Moderately high: men 95–102 cm; women 81–88 cm
High: men >102 cm; women >88 cm

Supplementary Table 4 Longitudinal association between BMI and WC, and pre-frailty/frailty among individuals with information on all five frailty criteria: The Tromsø Study 1994–2016

	Frailty status		Model 1	Model 2
	Robust (%) (n)	Pre-frail/frail (%) (n)	OR (95% CI)	OR (95% CI)
	70.4% (2016)	29.6% (848)		
BMI, kg/m^2				
Underweight	0.4 (8)	0.7 (6)	1.98 (0.67–5.84)	0.97 (0.28–3.23)
Normal	48.4 (976)	40.1 (340)	Ref.	Ref.
Overweight	42.8 (862)	42.9 (364)	1.19 (0.99–1.42)	1.18 (0.97–1.43)
Obesity	8.4 (170)	16.3 (168)	2.36 (1.82-–3.05)	2.28 (1.72-–3.01)
WC, cm	n = 600	n = 350		
Normal	53.3 (320)	40.9 (143)	Ref.	Ref.
Moderately high	31.3 (188)	34.0 (119)	1.40 (1.03–1.90)*	1.50 (1.08–2.08)*
High	15.3 (92)	25.1 (88)	2.15 (1.51–3.08)*	2.15 (1.46–3.18)*

Model 1: adjusted for age and sex (*excluding sex) at baseline.
Model 2: adjusted for age, sex, educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level (*excluding sex) at baseline.
BMI, body mass index; CI, confidence interval; OR, odds ratio; WC, waist circumference.

Supplementary Table 5 Cross- sectional association between BMI and WC, and pre-frailty/frailty: The Tromsø Study 2015–2016

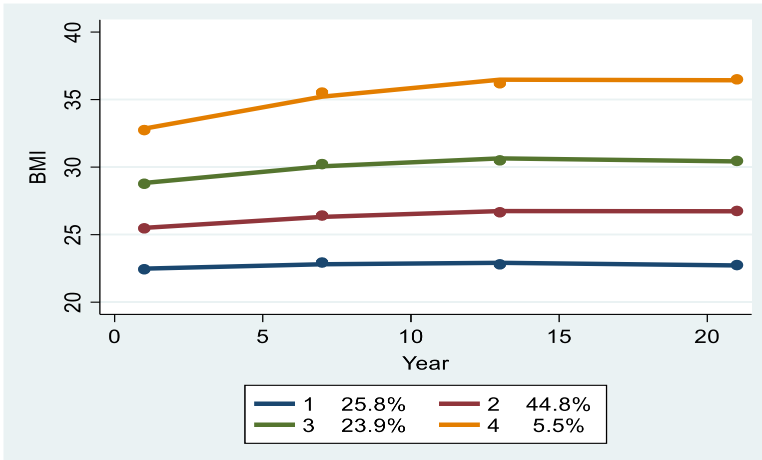
	Frailty status		Model 1	Model 2
	Robust (% (*n*))	Pre-frail/frail (% (*n*))	OR (95% CI)	OR (95% CI)
	70.5 (3179)	29.5 (1330)		
BMI, kg/m^2				
Underweight	0.5 (17)	1.4 (18)	2.93 (1.48–5.83)	2.32 (1.09–4.94)
Normal	30.0 (951)	24.5 (323)	Ref.	Ref.
Overweight	49.4 (1,566)	41.4 (547)	1.07 (0.91–1.26)	1.03 (0.86–1.23)
Obesity	20.1 (639)	32.7 (432)	2.14 (1.79–2.56)	1.88 (1.54–2.30)
WC, cm				
Normal	22.6 (716)	17.1 (225)	Ref.	Ref.
Moderately high	28.0 (888)	21.3 (281)	1.02 (0.83–1.25)*	1.01 (0.81–1.26)*
High	49.4 (1,569)	61.6 (812)	1.69 (1.42–2.01)*	1.45 (1.20–1.76)*

Model 1: minimally adjusted for age and sex (*excluding sex) at Tromsø7.
Model 2: adjusted for age, sex, educational level, smoking status, alcohol intake, comorbidities, social support, and self-perceived health (*excluding sex) at Tromsø7.
BMI, body mass index; CI, confidence interval; OR: odds ratio; WC, waist circumference.

SUPPLEMENTARY FIGURES

Supplemenatry Figure 1 Trajectories of individuals with repeated body mass index measurements between Tromsø4 and Tromsø7: The Tromsø Study 1994–2016.

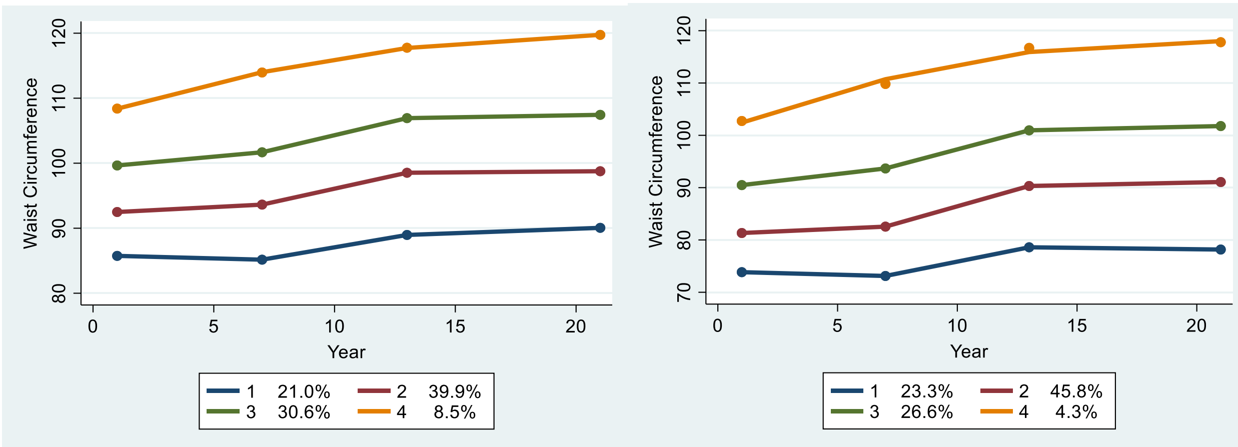
(n = 1,391)



Group 1	Stable normal weight	25.8%
Group2	Stable overweight	44.8%
Group 3	Overweight to obesity	23.9%
Group 4	Increasing obesity	5.5%

Supplementary Figure 2 Trajectories of individuals with repeated waist circumference measurements between Tromsø4 and Tromsø7: The Tromsø Study 1994–2016.

(Males: n = 731; females n = 660)



	Male	
Group 1	Stable normal WC	21.00%
Group 2	Stable moderately high WC	39.90%
Group 3	Moderately high to high WC	30.60%
Group 4	Increasing high WC	8.5 %

	Female	
Group 1	Stable normal WC	23.30%
Group 2	Moderately high to high WC	45.80%
Group 3	Gradually increasing high WC	26.60%
Group 4	Steeply increasing high WC	4.30%

Research checklist

	Item No	Content covered	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	√ (1-2)
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	√ (3)
Objectives	3	State specific objectives, including any pre-specified hypotheses	√ (3)
Methods			
Study design	4	Present key elements of study design early in the paper	√ (4)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	√ (4)
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed (*b*) Flow chart explaining inclusion and exclusion of partcipants	√ (4)
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	√ (4,5,6)
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	√ (4,5)
Bias	9	Describe any efforts to address potential sources of bias	√ (6)
Study size	10	Explain how the study size was arrived at	√ (4)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	√ (4,5,6)
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	√ (6)
Results			
Participants	13	(a) Information on participants	√ (4)
Descriptive data	14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	√ (7, 8)
Outcome data	15	Report numbers of outcome events or summary measures over time	√ (8-11)

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	√ (9-11)
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	√ (9-11)
Discussion			
Key results	18	Summarise key results with reference to study objectives	√ (11)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	√ (13)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	√ (11-14)
Generalisability	21	Discuss the generalisability (external validity) of the study results	√ (13-14)
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	√ (15)

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Body mass index and waist circumference as predictors of pre-frailty/frailty: The Tromsø study 1994–2016

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Body mass index and waist circumference as predictors of pre-frailty/frailty: The Tromsø study 1994−2016

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Keywords: body mass index, frailty, obesity, pre-frailty, waist circumference

Abstract

Objective: This study investigated the association between obesity, assessed using body mass index (BMI) and waist circumference (WC), and pre-frailty/frailty among older adults over 21 years of follow-up.

Design: Prospective cohort study.

Setting: Population-based study among community-dwelling adults in Tromsø municipality, Norway.

Participants: 2340 women and 2169 men aged ≥45 years attending the Tromsø Study in 1994–1995 (Tromsø4) and 2015–2016 (Tromsø7), with additional BMI and WC measurements in 2001 (Tromsø5) and 2007–2008 (Tromsø6).

Primary outcome measure: Physical frailty was defined as the presence of 3 or more and pre-frailty as the presence of 1-2 of the five frailty components suggested by Fried et al.: low grip strength, slow walking speed, exhaustion, unintentional weight loss and low physical activity.

Results: Participants with baseline obesity (adjusted odds ratio [OR] 2.41, 95% confidence interval [CI] 1.93–3.02), assessed by BMI, were more likely to be pre-frail/frail than those with normal BMI. Participants with high (OR 2.14, 95% CI 1.59–2.87) or moderately high (OR 1.57, 95% CI 1.21–2.03) baseline WC were more likely to be pre-frail/frail than those with normal WC. Those at baseline with normal BMI but moderately high/high WC or overweight with normal WC had no significantly increased odds for pre-frailty/frailty. However, those with both obesity and moderately high/high WC had increased odds of pre-frailty/frailty. Higher odds of pre-frailty/frailty was observed among those in "overweight to obesity" or "increasing obesity" trajectories than those with stable normal BMI. Compared with participants in a stable normal WC trajectory, those with high WC throughout follow-up were more likely to be pre-frail/frail.

Conclusion: Both general and abdominal obesity, especially over time during adulthood, is associated with an increased risk of pre-frailty/frailty in later years. Thus maintaining normal BMI and WC throughout adult life is important.

Strengths and limitations of this study:

1. This study has a long follow-up period of 21 years.
2. This study takes into account changes in body mass index (BMI) and waist circumference (WC) occurring through the follow-up period.
3. Frailty status was defined using a slightly modified version of Fried's physical frailty criteria.
4. Frailty and pre-frailty were combined as one outcome.
5. Information on frailty was only available at follow-up.

Background

Frailty is a dynamic multifactorial geriatric syndrome characterised by physiological deterioration, increased vulnerability and decreased resilience toward external stressors.[1,2] Frailty is associated with an increased risk of adverse events such as falls, disability, hospitalisation, reduced quality of life, and mortality.[1,2] It is preceded by pre-frailty, a multidimensional, transitional risk state.[3,4] Fried's frailty phenotype identifies pre-frailty as the presence of one or two and frailty as three or more of the five criteria: unintentional weight loss, self-reported exhaustion, weakness, slow walking speed, and low physical activity.[5] The prevalence of frailty and pre-frailty, defined using Fried's physical frailty measure,[5] among community-dwelling people aged ≥50 years across 62 countries, has been estimated to be 12% and 46%, respectively.[6]

Rapid population ageing has become a global phenomenon.[7] Ageing is typically associated with changes in body composition, such as decreased muscle mass and redistribution of total and regional fat.[8–10] Underweight older adults with minimal reserve capacity are at risk of adverse health outcomes[5,11], and unintentional weight loss is commonly acknowledged as a significant frailty indicator.[5] However, a growing body of evidence also suggests a positive association between obesity among older adults and the risk of frailty.[10,12–16] Obesity aggravates the age-related decline in muscle strength, aerobic capacity, and physical functionality, thus worsening health and well-being.[10,11,14,17,18] It is also closely associated with metabolic disorders, inflammaging and oxidative stress, all of which have been suggested to contribute to the risk of frailty.[14,19]

Anthropometric measures, including body mass index (BMI) and waist circumference (WC), are simple, cost-effective tools that reflect an individual's body composition and nutritional status. They are one of the widely used nutritional items for detecting frailty.[20] BMI indicates general obesity, while WC indicates abdominal obesity. When used together, they effectively assess obesity-related risks at the population level.[21–23] Some studies have detected a U-shaped association between BMI and frailty.[13,15,24] Midlife overweight and obesity, assessed by BMI, have been associated with the risk of pre-frailty and frailty in older age.[25,26] Similarly, a positive association between high WC and frailty among older adults has been observed in some studies.[9,16,27–29] These findings are even more relevant in the present context, where obesity prevalence is increasing across all age groups, posing a global public health challenge.[30]

Though the evidence is expanding, there have been limited longitudinal studies exploring and comparing the relationship of both BMI and WC with the risk of developing pre-frailty and frailty over a long follow-up period.[29] Few have explored changes in BMI[31,32] and its association with frailty, while studies that consider changes in WC in association with the development of frailty seem to be lacking. Therefore, the present study aimed to investigate the association of BMI and WC, separately and concurrently, with the risk of pre-frailty/frailty after 21 years of follow-up. Additionally, this study assessed changes in BMI and WC through the follow-up period and their association with pre-frailty/frailty.

Methods

The Tromsø study

This study uses data from the Tromsø study, an ongoing population-based study in the Tromsø municipality, Norway, consisting of seven surveys: Tromsø1 (1974), Tromsø2 (1979–1980), Tromsø3 (1986–1987), Tromsø4 (1994–1995), Tromsø5 (2001), Tromsø6 (2007–2008), and Tromsø7 (2015–2016). More than 45,000 women and men have participated in at least one of the surveys.[33] The earlier surveys (Tromsø1-Tromsø3) did not include WC measurements. Therefore, the present study uses data from Tromsø4 (baseline) to Tromsø7 (follow-up). Tromsø4 included 27,158 participants aged 25–97 years, Tromsø5, 8,130 participants aged 30–89 years, Tromsø6, 12,984 participants aged 30–87 years, and Tromsø7, 21,083 participants aged 40–99 years. The detailed information on the recruitment and the attendance of the participants has been described elsewhere.[33]

Study sample

The present study included Tromsø4 participants aged ≥45 years with valid information on BMI who also attended Tromsø7, i.e., 21 years of follow-up (n = 4,809). Participants with missing information on three or more frailty indicators in Tromsø7 were excluded (Figure 1). Our primary analytical sample had 4,509 participants. Out of these, 1,534 participants had information on WC at Tromsø4, and 1,391 had repeated measurements on both BMI and WC between Tromsø4 and Tromsø7.

Exposure

Bodyweight in kilograms and height in metres were measured wearing light clothes and no footwear. WC was measured using tape to the nearest centimetre at the umbilical level. All measurements were performed by trained personnel. BMI was calculated as the weight divided by the square of the height (kg/m^2) and categorised as underweight (<18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), and obesity (≥30.0 kg/m^2) according to the World Health Organization (WHO) criteria.[34] WC was categorised as normal (men ≤94 cm, women ≤80 cm), moderately high (men 95–102 cm, women 81–88 cm), and high (men>102 cm, women >88 cm) according to WHO.[35]

Frailty assessment

A modified version of Fried et al.'s frailty phenotype[5] was used to operationalise frailty in Tromsø7. Frailty was not operationalised at baseline as complete information on frailty indicators was unavailable. Five indicators were assessed at follow-up (Supplementary Table 1):

1. Unintentional weight loss: Self-reported involuntary weight loss during the last six months.[36]
2. Exhaustion: Response "pretty much" or "very much" to the question: "During the last week, have you experienced that everything is a struggle?" from the Hopkins' Symptom Checklist-10.[37]
3. Walking speed: Short Physical Performance Battery test, [38,39] where the fastest time out of two walks was selected and converted to seconds per 15 feet from seconds per 4 meters. Sex- and height-adjusted cut-offs, according to Fried et al.,[5] were used to identify participants with a low walking speed.
4. Weakness: Grip strength was measured using a newly calibrated Jamar+ Digital Dynamometer (Patterson Medical, Warrenville, IL, USA) following the Southampton protocol procedures.[40] Sex- and BMI-specific cut-offs suggested by Fried et al. [5] were used to identify participants with low grip strength.
5. Low physical activity: Response "Reading, watching TV/screen or other sedentary activity" to the question: "Describe your exercise and physical exertion in leisure time over the last year" from the Saltin–Grimby Physical Activity Level Scale for leisure-time physical activity.[41]

Participants were categorised as robust (0), pre-frail (1-2) and frail (≥3) based on the number of frailty indicators present.

Covariates

The potential covariates in this study were selected based on the existing knowledge and literature on frailty status. Sociodemographic characteristics included age, sex, educational level [primary/partly secondary education (up to 10 years of schooling), upper secondary education (minimum of 3 years), college/university short (<4 years), and college/university long (≥4 years)], and marital/cohabitation status (married/cohabiting or single/not cohabiting with a partner). Self-reported smoking status was categorised as current, former, or never smoker. Self-reported alcohol intake level was categorised as never-drinker, infrequent drinker (<2–4 times/month), and frequent drinker (>2–3 times/week). Comorbidity was defined using Charlson's comorbidity index[42] without weighting of the diseases. It was categorised as "no comorbidity" and "comorbidity" based on the self-reported presence of coronary heart disease (angina pectoris/myocardial infarction), stroke, diabetes, cancer, pulmonary disease (asthma/chronic bronchitis/emphysema), and peptic ulcer. Social support was categorised as self-reported "not enough good friends" or "enough good friends."

Self-perceived health status was categorised as "poor" or "good." Baseline physical activity level was categorised as no/low physical activity (0 hours/week spent in hard physical activity or ≤2 hours/week spent in light physical activity) and high physical activity (≥1 hour/week in hard physical activity or ≥3 hours/week in light physical activity).

Statistical analysis

The sociodemographic and lifestyle factors at baseline across robust and pre-frail/frail groups were described using mean and standard deviation for continuous variables and proportion and count for categorical variables. The differences between the two groups were tested using the student's *t*-test for continuous variables and the chi-square test for categorical variables.

Multivariable logistic regression analysis was used to assess the effect of BMI and WC on pre-frailty/frailty at follow-up. Five different longitudinal associations were assessed: baseline BMI and pre-frailty/frailty; baseline WC and pre-frailty/frailty; joint BMI and WC profile at baseline and pre-frailty/frailty; BMI trajectories and pre-frailty/frailty; WC trajectories and pre-frailty/frailty. The models were minimally adjusted for age and sex (Model 1) and further adjusted for educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level at baseline (Model 2). The adjustment variables were selected using a stepwise backward regression procedure. No significant collinearity or interaction was detected between covariates in the model.

Group-based trajectory modelling (GBTM) was conducted among 1,391 participants to assess changes in the BMI and WC throughout the 21-year follow-up period, with measurements on both BMI and WC available at Tromsø4, Tromsø5, Tromsø6 and Tromsø7. GBTM, also known as latent class growth analysis, is a semi-parametric technique that identifies distinct subgroups of individuals following a similar pattern of change over time on a given variable, using finite mixtures of defined probability distributions.[43] Different models with varying numbers of trajectory groups, varying functional forms and orders were compared. The most appropriate model was selected based on the Bayesian Information Criterion[44] and then introduced into longitudinal multivariable logistic regression models. The distinct BMI and WC trajectories were named based on their observed pattern. The WC trajectories were sex-stratified due to varying cut-off levels for men and women.

A new variable with five distinct strata (normal BMI and normal WC; normal BMI and moderately high/high WC; overweight and low WC; overweight and moderately high/high WC; obesity and moderately high/high WC) was formed by combining different categories of BMI and WC. They were then introduced into the multivariable models to assess the concurrent effects of BMI and WC on frailty status. While

forming the new joint variable, the underweight group was removed because of low prevalence (<1%), and moderately high and high WC groups were combined because of their low sample size when stratified.

Additional supplementary analyses were carried out. The cross-sectional association between BMI and WC level and frailty status at Tromsø7 was assessed. Since pre-frailty/frailty could not be assessed at baseline, the primary longitudinal analyses were repeated in a sub-population (*n*= 4,050), excluding participants aged 60 years and older at Tromsø4 who might have had an increased probability of being pre-frail/frail at that time point. The majority of the participants in the pre-frail/frail group had a frailty score of 1. In order to account for potential misclassification, analyses were performed on a further restricted sub-sample with a frailty score ≥2 at Tromsø7 (*n*= 3,124). The primary longitudinal analyses were also repeated among the subgroup of participants with non-missing information on all five frailty components (*n* = 2,864), and the association of obesity with each frailty component were assessed.

All the statistical analyses were conducted using STATA 16.[45] Statistical significance was set at $P < 0.05$. The results are expressed as adjusted odds ratios (ORs) with 95% confidence intervals (CIs).

Patient and public involvement

Patients and the public were not involved in this research's design, conduct, reporting, or dissemination plans.

Results

Study population

The mean age at baseline was 51.6 years, and the participants were followed up for 21 years. 28.4% of the participants were pre-frail, 1.1% were frail, and 70.5% were robust at follow-up (Table 1). In total, 50.6% of the robust group and 55.0% of the pre-frail/frail group were women. Most robust and pre-frail/frail participants were either married or cohabiting (84.3% and 80.3%) and reported having enough good friends (83.1% and 80.5%) at baseline. All the baseline characteristics, except comorbidity, were significantly different in the robust and the pre-frail/frail groups (Table 1).

When assessed at follow-up, all the sociodemographic, lifestyle and disease-related factors were significantly associated with pre-frailty/frailty (Supplementary Table 2). When the eligible participants lost to follow-up (*n* = 8,649) were compared with the attendees, they were found to be older (mean age 63.2 years) with a less healthy lifestyle and higher comorbidities (Supplementary Table 3).

BMI and WC

At baseline, the proportion of individuals with underweight was low (<1%) (Table 2). The proportion of individuals with normal BMI was higher among the robust group than the pre-frail/frail group (47.6% versus 39.3%), whereas the proportion of individuals with obesity was higher among the pre-frail/frail group (17.1% versus 8.4%). The robust group had a higher proportion of individuals with normal WC than the pre-frail/frail group (51.5% versus 37.3%), whereas the pre-frail/frail group had a higher proportion of individuals with high WC (27.7% versus 17.4%). A similar distribution of different BMI and WC categories across robust and pre-frail/frail groups was observed at follow-up (Supplementary Table 2). Both robust and pre-frail/frail groups at follow-up had an increased proportion of individuals with obesity and high WC compared with baseline (Table 2; Supplementary Table 2).

Table 1 Baseline characteristics of participants by frailty status at follow-up: The Tromsø Study 1994–2016

	Frailty status		
	Robust (% (*n*)) 70.5 (3,179)	**Pre-frail/frail (% (*n*)) 29.5 (1,330)**	***P* value**
Age in years, mean (SD)	51.1 (5.1)	52.8 (5.9)	0.000[a]
Women	50.6 (1,608)	55.0 (732)	0.006
Smoking status			
Current smokers	27.0 (858)	33.7 (448)	
Former smokers	36.1 (1,149)	34.0 (452)	0.001
Never	36.9 (1,172)	32.3 (430)	
High physical activity level	69.5 (2,210)	56.9 (756)	0.001
Married or cohabiting	84.3 (2,679)	80.3 (1,068)	0.001
Self-perceived health – good	75.4 (2,394)	61.5 (818)	<0.001
Social support – enough good friends	83.1 (2,404)	80.5 (976)	0.041
Educational level			
Primary/Partly secondary	32.8 (1,041)	42.4 (562)	
Upper secondary	34.3 (1,085)	34.2 (453)	<0.001
College/University short	16.5 (524)	12.8 (169)	
College/University long	16.4 (520)	10.6 (141)	
Alcohol intake			
Never/Abstaining	9.0 (286)	11.9 (158)	
Infrequent drinker	76.2 (2,419)	76.6 (1,015)	<0.001
Frequent drinker	14.8 (468)	11.5 (152)	
Prevalent diseases			
Pulmonary disease[b]	8.6 (272)	9.5 (126)	0.323
Coronary heart disease[c]	2.3 (73)	4.5 (59)	<0.001
Diabetes	0.4 (12)	0.6 (8)	0.300
Cancer	2.8 (79)	3.5 (42)	0.210
Stroke	0.6 (19)	0.8 (11)	0.386
Peptic ulcer	7.0 (197)	8.9 (105)	0.033
Comorbidity	1.9 (59)	2.7 (36)	0.070

Values are percentages (numbers); *P* value: χ^2 test for categorical variables; *P* value: [a]Student's t-test; [b]including asthma/chronic bronchitis/emphysema; [c]including angina pectoris/myocardial infarction.

When BMI and WC level was assessed jointly at baseline (Table 3), the robust group had a higher proportion of individuals with both BMI and WC in the normal range than the pre-frail/frail group (36.1% versus 29.1%). The proportion of individuals with both obesity and moderately high/ high WC was higher among the pre-frail/frail group (16.9% versus 7.4%).

The GBTM resulted in four distinct trajectories of BMI (*n* = 1391): stable normal BMI (25.8%), stable overweight (44.8%), overweight to obesity (23.9%), and increasing obesity (5.5%) (Supplementary Figure 1). The increasing obesity trajectory included individuals with BMI ≥30 kg/m² at baseline, which kept increasing to a higher obesity level, i.e., BMI ≥35 kg/m². Four distinct WC trajectories were identified for both women (*n* = 660) and men (*n* = 731) (Supplementary Figure 2). The WC trajectories for women were: stable normal WC (23.3%), moderately high to high WC (45.8%), gradually increasing high WC (26.6%), and steeply increasing high WC (4.3%). The WC trajectories for men were: stable normal WC (21.0%), stable moderately high WC (39.9%), moderately high to high WC (30.6%), and increasing high WC (8.5%).

BMI, WC, and pre-frailty/frailty

Individuals who had obesity (OR 2.41, 95% CI 1.93–3.02) or overweight (OR 1.19, 95% CI 1.02–1.39) at baseline had significantly higher odds of becoming pre-frail/frail at follow-up compared with individuals with normal BMI (Model 2, Table 2). No statistically significant association was detected between underweight group and the odds of pre-frailty/frailty; however, the number of underweight individuals was insufficient to reach any conclusion. Participants with moderately high WC (OR 1.57, 95% CI 1.21–2.03) or high WC (OR 2.16, 95% CI 1.59–2.87) at baseline had higher odds of becoming pre-frail/frail at follow-up compared to individuals with a normal WC (Model 2, Table 2).

The supplementary cross-sectional analysis (Supplementary Table 4) indicated a significant association between obesity and pre-frailty/frailty among older adults (OR 1.88, 95% CI 1.54–2.30), whereas no association was detected between overweight and pre-frailty/frailty. As for WC, only high WC was associated with increased odds of pre-frailty/frailty (OR 1.45, 95% CI 1.20–1.76) in the cross-sectional analysis.

Table 2 Longitudinal association between BMI and WC, and pre-frailty/frailty: The Tromsø Study 1994–2016

	Frailty status			
	Robust (% (*n*))	**Pre-frail/frail (% (*n*))**	**Model 1 OR (95% CI)**	**Model 2 OR (95% CI)**
	70.5 (3179)	29.5 (1330)		
BMI, kg/m²				
Underweight	0.3 (11)	0.7 (9)	2.15 (0.88–5.29)	1.32 (0.49–3.54)

Normal	47.6 (1,513)	39.3 (522)	Ref.	Ref.
Overweight	43.7 (1,388)	43.0 (572)	1.18 (1.02–1.36)	1.19 (1.02–1.39)
Obesity	8.4 (267)	17.0 (227)	2.42 (1.98–2.98)	2.41 (1.93–3.02)
WC, cm	*n* = 952	*n* = 582		
Normal	51.5 (490)	37.3 (217)	Ref.	Ref.
Moderately high	31.1 (296)	35.0 (204)	1.54 (1.21–1.96)*	1.57 (1.21–2.03)*
High	17.4 (166)	27.7 (161)	2.16 (1.65–2.83)*	2.14 (1.59–2.87)*

Model 1: adjusted for age and sex (*excluding sex) at baseline.
Model 2: adjusted for age, sex, educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level (*excluding sex) at baseline.
BMI, body mass index; CI, confidence interval; OR: odds ratio; WC, waist circumference.

BMI categories
Underweight: <18.5 kg/m^2
Normal: 18.5–24.9 kg/m^2
Overweight: 25.0–29.9 kg/m^2
Obesity: ≥30 kg/m^2

WC categories
Normal: men ≤94 cm; women ≤80 cm
Moderately high: men 95–102 cm; women 81–88 cm
High: men >102 cm; women >88 cm

The longitudinal model that included joint BMI and WC profile at baseline showed that participants who had overweight with moderately high/high WC (OR 1.48, 95% CI 1.11–1.98) or participants who had obesity with moderately high/high WC (OR 3.11, 95% CI 2.07–4.70) had higher odds of being pre-frail/frail compared with participants with normal BMI and normal WC (Model 2, Table 3). No significant association with pre-frailty/frailty was detected among participants who had normal BMI with moderately high/high WC or overweight with normal WC at baseline.

The sensitivity analyses restricted to participants with baseline age <60 years (Supplementary Table 5) and further restricted to those with a frailty score ≥2 at follow-up (Supplementary Table 6) confirmed the higher odds of pre-frailty/frailty among participants with baseline obesity and/or moderately high/ high WC. However, no significant association was detected between participants in overweight category and pre-frailty/frailty. The sensitivity analysis among participants with complete information on all five frailty components (Supplementary Table 7) also generated similar results.

Table 3 Association between combined BMI and WC profiles, and pre-frailty/frailty: The Tromsø Study 1994–2016

	Frailty status			
Longitudinal	**Robust (% (*n*))**	**Pre-frail/frail (% (*n*))**	**Model 1 OR (95% CI)**	**Model 2 OR (95% CI)**
BMI and WC profile, baseline	62.8 (870)	37.2 (515)		
Normal BMI and normal WC	36.1 (314)	29.1 (150)	Ref.	Ref.
Normal BMI and moderately high/high WC	8.4 (73)	8.0 (41)	1.13 (0.73–1.74)	1.01 (0.63–1.61)
Overweight and normal WC	15.9 (139)	9.5 (49)	0.74 (0.50–1.08)	0.79 (0.53–1.19)
Overweight and moderately high/high WC	32.2 (280)	36.5 (188)	1.40 (1.07–1.84)	1.48 (1.11–1.98)
Obesity and moderately high/high WC	7.4 (64)	16.9 (87)	2.86 (1.96–4.18)	3.11 (2.07–4.70)

Model 1: adjusted for age at baseline.
Model 2: adjusted for age, educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level at baseline.

BMI, body mass index; CI, confidence interval; OR: odds ratio; WC, waist circumference.

The model with BMI trajectories (Model 2, Table 4) indicated higher odds of pre-frailty/frailty among participants in the overweight to obesity trajectory (OR 1.67, 95% CI 1.19–2.35) or those in the constantly increasing obesity trajectory (OR 3.12, 95% CI 1.80–5.41), compared with those in the stable normal BMI trajectory. Contrarily, there was no significant association in the stable overweight category. The model with WC trajectories (Model 2, Table 4) showed that women in the gradually increasing high WC trajectory (OR 2.17, 95% CI 1.32–3.59) or the steeply increasing high WC trajectory (OR 4.09, 95% CI 1.54–10.90) had higher odds of being pre-frail/frail compared with women in the normal WC trajectory. Similarly, men in the increasing high WC trajectory (OR 3.36, 95% CI 1.71–6.59) had higher odds of pre-frailty/frailty compared with men in the normal WC trajectory. The same trend in the association between different BMI and WC trajectories and pre-frailty/frailty was observed in sensitivity analyses restricted to participants with baseline age <60 years (Supplementary Table 5).

When the association was assessed separately for each frailty component (Supplementary Table 8), overweight or obesity at baseline was associated with higher odds of slow walking speed, low physical activity and low grip strength at follow-up. However, the association between BMI and grip strength was no longer significant in the fully adjusted model. Moderately high or high WC at baseline was associated with higher odds of slow walking speed and low physical activity.

Table 4 Association between BMI and WC trajectories and pre-frailty/frailty: The Tromsø study 1994–2016

	Frailty status		Model 1	Model 2
	Robust (% (*n*))	Pre-frail/frail (% (*n*))	OR (95% CI)	OR (95% CI)
	62.8 (874)	37.2 (517)		
BMI trajectories				
Stable normal BMI	27.8 (243)	22.4 (116)	Ref.	Ref.
Stable overweight	46.6 (407)	42.4 (219)	1.20 (0.91–1.59)	1.21 (0.90–1.62)
Overweight to obese	21.8 (191)	26.5 (137)	1.62 (1.18–2.22)	1.67 (1.19–2.35)
Increasing obesity	3.8 (33)	8.7 (45)	3.07 (1.85–5.09)	3.12 (1.80–5.41)
	59.4 (392)	40.6 (268)		
WC trajectories (women)				
Stable normal WC	26.3 (103)	17.5 (47)	Ref.	Ref.
Moderately high to high WC	49.7 (195)	42.5 (114)	1.27 (0.84–1.94)*	1.30 (0.83–2.05)*
Gradually increasing high WC	20.9 (82)	33.6 (90)	2.34 (1.47–3.70)*	2.17 (1.32–3.59)*
Steeply increasing high WC	3.1 (13)	6.3 (17)	3.04 (1.34–6.90)*	4.09 (1.54–10.90)*
	65.9 (482)	34.1 (249)		
WC trajectories (men)				
Stable normal WC	22.4 (108)	18.1 (45)	Ref.	Ref.
Stable moderately high WC	41.1 (198)	38.5 (96)	1.18 (0.77–1.80)*	1.12 (0.72–1.76)*
Moderately high to high WC	31.5 (152)	28.9 (72)	1.18 (0.75–1.85)*	1.12 (0.69–1.79)*
Increasing high WC	5.0 (24)	14.5 (36)	3.73 (1.99–6.97)*	3.36 (1.71–6.59)*

Model 1: adjusted for age and sex at baseline (*adjusted for age only).

Model 2: adjusted for age, sex, educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level (*excluding sex) at baseline.
BMI, body mass index; CI, confidence interval; OR: odds ratio; WC, waist circumference.

Discussion

The present study followed 4,509 community-dwelling participants from the population-based Tromsø Study from 1994 to 2016 to examine the association between general and abdominal obesity and the risk of frailty. This study suggests an increased likelihood of pre-frailty/frailty among those with baseline obesity. Increased likelihood of pre-frailty/frailty was also observed among those with high or moderately high WC at baseline. When assessed jointly, participants with both obesity and moderately high/high WC at baseline had increased odds of being pre-frail/frail compared to those with BMI and WC in the normal range. Participants in the "overweight to obesity" or the "increasing obesity" trajectories had increased odds of pre-frailty/frailty compared with those in the stable normal BMI trajectory. Additionally, participants with a high WC at baseline, whose WC gradually or steeply increased throughout the follow-up period, had increased odds of being pre-frail/frail compared with those in a stable normal WC trajectory.

Our conclusions align with the findings from two previous longitudinal studies with a similar follow-up period (26 and 22 years) that reported a significant positive association between midlife overweight or obesity and the development of pre-frailty and frailty in later life.[25,26] However, we should be cautious while interpreting the association between baseline overweight BMI and pre-frailty/frailty. In our study, this association was not significant in the sensitivity analyses where we excluded participants aged 60 years and older at baseline. A prospective study with a follow-up period of 3.5 years observed a significantly increased risk of frailty among underweight women and women with overweight and obesity.[24] No significant association between baseline underweight status and risk of pre-frailty/frailty was detected in our study. However, the number of underweight individuals in our study was too low, resulting in a low statistical power to reach any conclusion. In terms of WC and frailty status, similar to our results, a positive association between higher WC and frailty among older adults was reported by a 3.5-year follow-up study from two prospective Spanish cohorts.[29] A positive association between high WC and frailty was observed in a few other studies;[9,16,27] however, they were cross-sectional and used slightly different cut-offs to categorise WC. We identified BMI and WC trajectories to account for the dynamic change in the adiposity level that might occur during adulthood. In line with our findings regarding BMI trajectories, comparable trajectories and observations about a higher risk of pre-frailty and frailty among those with increasing BMI were observed in a 26-year follow-up study.[32] A large study that followed adults aged ≥51 years for ten years reported a higher incidence of frailty among weight gain class, weight loss class, and consistent obesity class.[31] Literature on long-term changes in WC and its association with frailty seems lacking. Few epidemiological studies have explored the combined effect of BMI and WC on frailty among older adults. Two studies conducted among adults aged ≥65 years in Portugal[46] and ≥60 years in Spain[29] observed a positive association between frailty and adiposity only when the individuals had both a high WC and a high BMI. It aligns with our results to a certain extent, as we observed an increased likelihood of pre-frailty/frailty among individuals with both obesity and moderately high/high WC at baseline. We also observed higher odds of pre-frailty/frailty among those who had overweight with a moderately high/high WC at baseline. However, this association was not significant in the sensitivity analyses where we excluded participants aged 60 years and older at baseline. On the contrary, high WC was reported to be associated with frailty regardless of their BMI categories by two cross-sectional studies conducted among community-dwelling adults aged ≥65 years in China[27] and England,[15] indicating WC to be better linked with frailty. Notably, participants who had normal BMI with moderately high/high WC or those who had overweight with normal WC did not have significantly increased odds of pre-frailty/frailty in our study. This finding indicates the importance of considering both BMI and WC to identify the risk of frailty.

There are different mechanisms through which obesity might contribute to pre-frailty/frailty. Increased adiposity leads to increased secretion of pro-inflammatory adipokines, thus contributing to inflammation,[14,19] which is also associated with frailty among older adults.[47] Obesity leads to increased fat mass and increased lipid infiltration in muscle fibres resulting in reduced muscle strength and function.[14,48] When coupled with an age-related decline in muscle mass and strength, it causes "sarcopenic obesity", which is linked to an increased risk of frailty and disability.[19,49,50] Grip strength, often used as a proxy for muscle strength in older adults, was found to be associated with baseline overweight and obesity assessed using BMI in our study. However, the association was no longer significant when further adjusted for potential covariates. Slow walking speed and low physical activity, which often represent lower physical functioning at an older age, were significantly associated with baseline BMI and WC. The primary strength of this study is its prospective design with a long follow-up period of two decades. However, several changes in participant's lifestyle, diet, habits, and physical and psycho-social environments might have occurred during this period. We could not account for these factors, which potentially impacted the development of pre-frailty/frailty. So, the result of this study should be cautiously interpreted in light of these contextual issues. We used BMI and WC to define general and abdominal obesity. BMI is often criticised for its inability to provide information on fat distribution,[22] while WC is criticised for its limitation in distinguishing between visceral and subcutaneous fat.[51] However, they are effective in assessing obesity-related risks at the population level.[21,22] A study among Tromsø7 participants aged ≥40 years found a strong correlation between BMI and visceral adipose tissue (VAT) mass and WC and VAT mass. It also concluded them to be a satisfactory substitute to identify cardiometabolic risk.[23] Further, they are simple to measure, easy to replicate, and widely used in routine health assessments, thus, helping identify individuals at risk of frailty to provide timely interventions. The repeated measures on BMI and WC allowed us to account for changes in participants' obesity status through the follow-up period and gain a comprehensive understanding of the long-term effects of these exposures on the risk of frailty in later life. However, we could not account for the development and change in frailty status that might have occurred over time as repeated measures on frailty were unavailable. Our outcome was physical frailty, assessed using Fried et al.'s frailty phenotype definition.[5] Though widely used,[52] it defines frailty from the unidimensional perspective of reduced physical functioning and declining physiological reserves. In the context where frailty is being recognised as a multidimensional construct encompassing not just physical but also cognitive, social and psychological dimensions [53], the scope of our results focusing just on physical aspects of frailty might be limited. This study's objectively measured physical frailty components (low grip strength and low walking speed) aligned with Fried's definition; however, the questionnaires for self-reported components (exhaustion, low physical activity and unintentional weight loss) varied slightly. Each frailty indicator we utilised has been validated in different research contexts.[36–38,41] The self-reported frailty components are nevertheless prone to information bias. A systematic review that investigated 262 physical frailty phenotypes acknowledged that modifications in the definition of frailty phenotype are common and have an important impact on the classification and predictive ability of the definition.[54] A fair agreement has been reported between Fried's definition and the completely questionnaire-based physical frailty definition.[55,56]

The main limitation of our study is the selection bias resulting from differential loss to follow-up. Those lost to follow-up were comparatively older and had a higher proportion of general and abdominal obesity and other potential risk factors for frailty. This might have led to a lower prevalence of frailty in Tromsø7. In total, 1.1% of the participants aged ≥66 years at Tromsø7 were frail, and 28.4% were pre-frail which is much lower than the pooled prevalence estimates provided by O'Caoimh et al.[6] It aligns with the findings from a study where the grip strengths of Tromsø7 participants and Russian Know Your Heart study participants aged 40-69 years were compared. The average Norwegian participant had a mean grip strength comparable to a seven-year younger Russian counterpart.[57] This indicates that the nordic population might be comparatively healthier,[58] thus limiting the generalisability of our findings to other populations across the globe. Only a sub-sample of our study population had information on both BMI and WC, and an even lower number had repeated measurements available for both exposures. Therefore, the models including both BMI and WC might have low statistical power, particularly when considering the repeated measures. Information on frailty measures was not available at baseline. However, most participants were in their mid-life (median age 50) at baseline, lowering their likelihood of having frailty components. The sensitivity analyses, where we excluded participants aged ≥60 years from baseline as a proxy for exclusion of pre-frail/frail individuals, showed a similar trend in the association between baseline obesity, assessed using BMI and WC, and pre-frailty/frailty at an older age. We adjusted for several confounding factors; however, the potential for residual confounding remains. Most covariates in our study, including comorbidity, were self-reported.

We combined pre-frailty and frailty as a single outcome because of the low frailty prevalence in this study. The pre-frail/frail population in this study is primarily pre-frail with a frailty score of 1, half of which were the ones with low physical activity. So, misclassification of comparatively healthier but less active participants with severely pre-frail/frail participants might have occurred. The sensitivity analyses on participants with ≥2 frailty score, which mostly supported results from the primary analysis, addressed this issue to some extent. It would have been informative to assess the association with pre-frailty and frailty separately. Nevertheless, understanding factors associated with pre-frailty is highly relevant because pre-frailty is gaining broader interest as an ideal opportunity for administering timely intervention to delay or reverse frailty and the associated adverse outcomes.[59] Of note, as our outcome pre-frailty/frailty is common, the OR estimates obtained might slightly overestimate the relative risk, and caution should be applied while interpreting it as a risk.

In the context where the population is rapidly ageing and the obesity epidemic is rising, growing evidence recognises the subgroup of "fat and frail" older individuals in contrast to viewing frailty only as a wasting disorder.[12,15,26] In this study, participants with both high BMI and high WC, i.e., general and abdominal obesity, especially for a long duration throughout their adulthood, were observed to have an increased likelihood of pre-frailty/frailty. It highlights the importance of routinely assessing and maintaining optimal BMI and WC throughout adulthood to lower the risk of frailty in older age.

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Competing Interest

None declared.

Ethical approval

The Tromsø Study was approved by the Regional Committee of Medical and Health Research Ethics (REK) North and the Norwegian Data Protection Authority. Approvals from REK (ref. 2021/234146) and the Norwegian Centre for Research Data (NSD) (ref. 364331) were obtained for this particular study.

Contributions

SU was responsible for conceptualisation, data acquisition, analysis, interpretation, writing original draft, review and editing; LFA was responsible for conceptualisation, funding acquisition, supervision, writing critical review and editing; LAH was responsible for data acquisition for the Tromsø Study, constant coordination, writing critical review and editing; AH was responsible for conceptualisation, funding acquisition, data acquisition, supervision, writing critical review and editing.

Data availability statement

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 can be made available from the Tromsø Study upon application to 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 <mailto:tromsous@uit.no>.

Patient consent for publication

Not required

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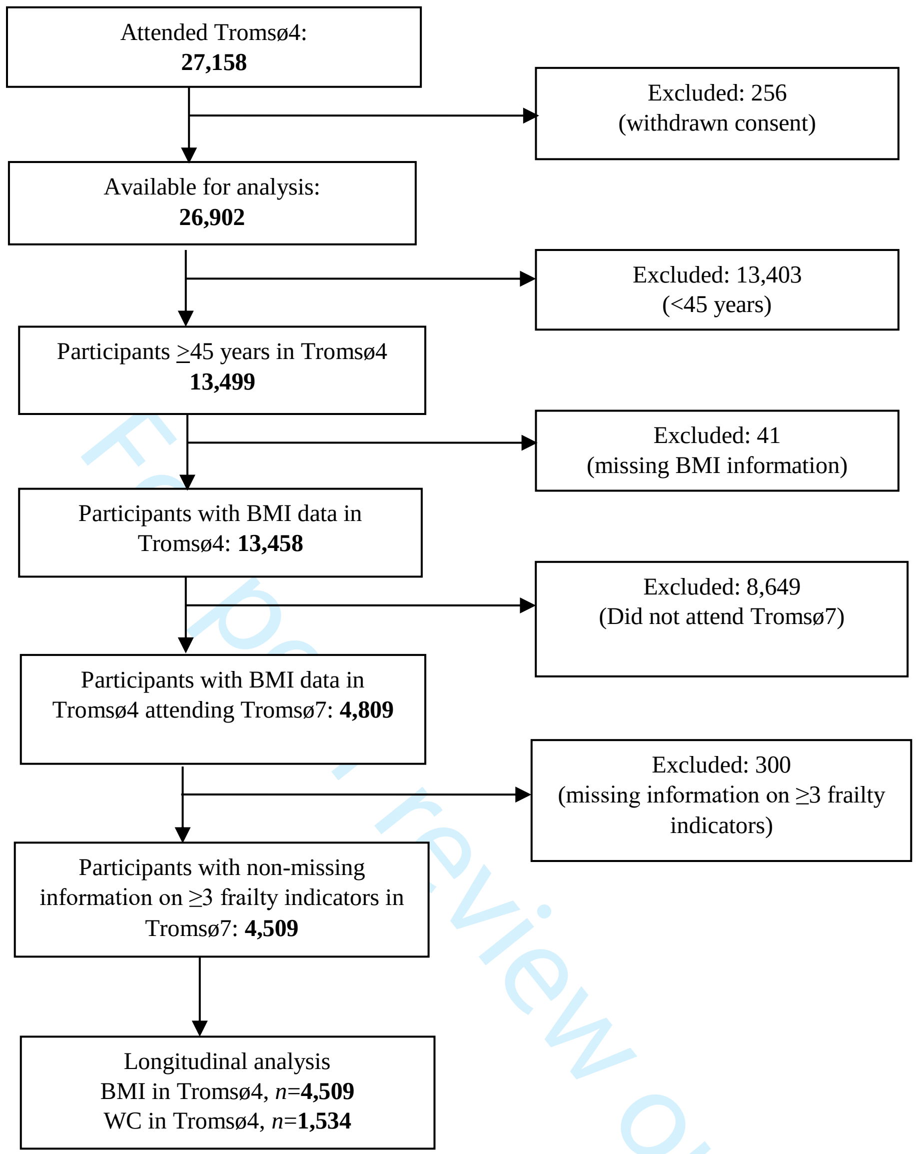


Figure 1 Flowchart displaying participants' inclusion and exclusion

SUPPLEMENTARY TABLES

Supplementary Table 1 Comparison between Fried et al.'s suggested criteria for frailty and modified frailty indicators used in this study

Frailty	Fried et al. (2001)	Current study
Exhaustion	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 day? 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 time (3–4 days) 3 = Most of the time **Exhausted: "A moderate amount of time (3–4 days)" or "Most of the time"**	Hopkins Symptom Checklist (HSCL-10): During the last week, have you experienced that everything is a struggle? 1 = No complaint 2 = Little complaint 3 = Pretty much 4 = Very much **Exhausted: "Pretty much" or "Very much"**
Physical activity	Minnesota Leisure Time Activity Questionnaire asking about walking, chores (moderately strenuous), mowing the lawn, raking, gardening, hiking, jogging, biking, exercise, cycling, dancing, aerobics, bowling, golf, singles, tennis, racquetball, calisthenics, swimming. The kcal/week expended was calculated using a standardized algorithm. Lowest 20% were identified, resulting in following cut-off for frailty: Men: <383 kcal of physical activity/week Women: <270 kcal of physical activity/week	Describe your exercise and physical exertion in leisure time over the last year (Saltin & Grimby's Scale). 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 shoveling, etc. at least 4 hours a week 4 = Participation in hard training or sports competitions, regularly several times a week **Low physical activity level: "Reading, watching TV/screen or other sedentary activity"**
Weight loss	In the last year, have you lost more than 10 pounds (4.5 kg) unintentionally (not due to dieting or exercise)? **Frail: "Yes"**	Have you involuntarily lost weight during the last 6 months? (Malnutrition Universal Screening Tool) 0 = No 1 = Yes **Lost weight: "Yes"**
Grip strength	Measured by Jamar dynamometer (kg) Maximal strength in dominant hand (3 trials) Stratified by sex and BMI quartiles. Lowest 20% were identified, resulting in the following cut-off for frailty: **Men** — **Cut-off for grip strength (kg) criterion for frailty** BMI ≤24 — ≤29 kg BMI 24.1–26 — ≤30 kg BMI 26.1–28 — ≤30 kg BMI >28 — ≤32 kg **Women** BMI ≤23 — ≤17 kg BMI 23.1–26 — ≤7.3 kg BMI 26.1–29 — ≤18 kg BMI >29 — ≤21 kg	Measured by Jamar dynamometer (kg) Strongest measurement from 3 trials in each hand Stratified by sex and BMI quartiles as per Fried's definition: **Men** — **Cut-off for grip strength (kg) criterion for frailty** BMI ≤24 — ≤29 kg BMI 24.1–26 — ≤30 kg BMI 26.1–28 — ≤30 kg BMI >28 — ≤32 kg **Women** BMI ≤23 — ≤17 kg BMI 23.1–26 — ≤17.3 kg BMI 26.1–29 — ≤18 kg BMI >29 — ≤21 kg

Frailty	Fried et al. (2001)	Current study
Walking speed	Time to walk (seconds) 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 frailty: **Men** **Cut-off for walking speed criterion for frailty** Height ≤173 cm ≥7 s Height >173 cm ≥6 s **Women** Height ≤159 cm ≥7 s Height >159 cm ≥6 s	SPPB: Short Physical Performance Battery – walking test Fastest of two times (seconds) to walk 4 m stratified by sex and height according to Fried's gender-specific cut-off. Converted to feet from meters. **Men** **Cut-off for walking speed criterion for frailty** Height ≤173 cm ≥7 s Height >173 cm ≥6 s **Women** Height ≤159 cm ≥7 s Height >159 cm ≥6 s
Frailty status	Frailty score: 0 = Robust 1–2 = Pre-frail ≥3 = Frail	Frailty score: 0 = Robust 1–2 = Pre-frail ≥3 = Frail Pre-frailty/frailty score: 0 = Robust ≥1 = Pre-frail/frail

Supplementary Table 2 Descriptive characteristics of participants at follow-up: The Tromsø Study 2015-2016

	Frailty status		
	Robust (% (n)) 70.5 (3,179)	**Pre-frail/ frail (% (n)) 29.5 (1,330)**	***P* value**
Age in years, mean (SD)	72.1 (5.1)	73.8 (5.9)	<0.001[a]
Women	50.6 (1608)	55.0 (732)	0.006
Smoking status			
Current smokers	8.3 (262)	14.4 (188)	
Former smokers	53.2 (1,674)	50.8 (666)	<0.001
Never	38.4 (1,208)	34.8 (456)	
Married or cohabiting	71.0 (2,258)	64.6 (859)	<0.001
Self-perceived health – good	69.4 (2,178)	43.2 (566)	<0.001
Social support – enough good friends	87.4 (2,676)	82.0 (1,047)	<0.001
Educational level			
Primary/Partly secondary	39.1 (1,201)	50 (632)	
Upper secondary	26.6 (817)	26.2 (331)	<0.001
College/University short	16.3 (500)	12.2 (154)	
College/University long	18.1 (556)	11.6 (147)	
Alcohol intake			
Never/Abstaining	11.2 (352)	17.4 (229)	
Infrequent drinkers	58.6 (1,846)	61.0 (803)	<0.001
Frequent drinkers	30.3 (954)	21.6 (284)	
Prevalent diseases			
Pulmonary disease[b]	14.6 (444)	19.9 (250)	<0.001
Coronary heart disease[c]	13.7 (415)	19.3 (241)	<0.001
Diabetes	7.3 (224)	14.8 (186)	<0.001
Cancer	15.6 (475)	19.3 (243)	0.003
Stroke	5.1 (154)	8.1 (101)	<0.001
Peptic ulcer	–	–	<0.001
Comorbidity	89.8 (2,800)	82.4 (1,075)	<0.001
BMI categories			
Underweight	0.5 (17)	1.4 (18)	
Normal	30.0 (951)	24.5 (323)	<0.001
Overweight	49.4 (1,566)	41.4 (547)	
Obese	20.1 (639)	32.7 (432)	
WC categories			
Normal	22.6 (716)	17.1 (225)	
Moderately high	28.0 (888)	21.3 (281)	<0.001
High	49.4 (1,569)	61.6 (812)	

Values are percentage (number); P value: χ^2 test for categorical variables P value: [a]Student's t-test; [b]including asthma/chronic bronchitis/emphysema; [c]including angina pectoris/myocardial infarction. BMI, body mass index; WC, waist circumference.

BMI categories
Underweight: <18.5 kg/m^2
Normal: 18.5–24.9 kg/m^2
Overweight: 25.0–29.9 kg/m^2
Obesity: ≥30 kg/m^2

WC categories
Normal: men ≤94 cm; women ≤80 cm
Moderately high: men 95–102 cm; women 81–88 cm
High: men >102 cm; women >88 cm

Supplementary Table 3 Descriptive baseline characteristics of Tromsø4 participants who attended Tromsø7 versus those who did not: The Tromsø Study 1994–2016

	Frailty status		
	Not attended Tromsø7 n = 8,649 (% (n))	Attended Tromsø7 n = 4,809 (% (n))	*P* value
Age in years, mean (SD)	63.2 (11.0)	52.0 (5.8)	<0.001[a]
Women	52.4 (4,533)	52.4 (2520)	0.990
Smoking status			
Current smokers	33.7 (2,916)	29.4 (1,414)	
Former smokers	33.4 (2,886)	35.6 (1,714)	<0.001
Never	32.9 (2,847)	(34.9) 1,681	
Married or cohabiting	64.7 (5,568)	(82.7) 3,977	<0.001
Self-perceived health status – good	50.7 (4,378)	(70.3) 3,379	<0.001
Social support – enough good friends	83.0 (5,775)	(82.2) 3,590	0.330
Educational level			
Primary/Partly secondary	57.2 (4,911)	(36.9) 1,768	
Upper secondary	27.5 (2,362)	(34.1) 1,633	<0.001
College/University short	8.1 (696)	(14.9) 716	
College/University long	7.2 (622)	(14.1) 678	
Alcohol intake			
Never/Abstaining	24.5 (2,108)	(10.2) 491	
Infrequent drinkers	66.8 (5,749)	(76.2) 3655	<0.001
Frequent drinkers	8.7 (744)	(13.5) 649	
Prevalent diseases			
Pulmonary disease[b]	16.2 (1,097)	(9.9) 430	<0.001
Coronary heart disease[c]	14.8 (1,281)	(3.1) 149	<0.001
Diabetes	4.3 (374)	(0.5) 25	<0.001
Cancer	7.7 (517)	(3.1) 132	<0.001
Stroke	3.7 (318)	(0.7) 33	<0.001
Ulcer	14.1 (908)	(7.8) 333	<0.001
Comorbidity	9.9 (858)	(2.3) 36	<0.001
BMI categories			
Underweight	1.7 (149)	0.5 (22)	
Normal	40.0 (3,463)	44.9 (2,169)	<0.001
Overweight	42.3 (3,659)	43.5 (2,094)	
Obesity	15.9 (1,378)	11.1 (533)	
WC categories			
Normal	39.0 (1,784)	45 (765)	
Moderately high	29.7 (1,356)	32.6 (554)	<0.001
High	31.3 (1,434)	22.4 (381)	

Values are percentage (number); P value: χ^2 test for categorical variables P value: [a]Student's t-test; [b]including asthma/chronic bronchitis/emphysema; [c]including angina pectoris/myocardial infarction. BMI, body mass index; WC, waist circumference.

BMI categories
Underweight: <18.5 kg/m^2
Normal: 18.5–24.9 kg/m^2
Overweight: 25.0–29.9 kg/m^2
Obesity: ≥30 kg/m^2

WC categories
Normal: men ≤94 cm; women ≤80 cm
Moderately high: men 95–102 cm; women 81–88 cm
High: men >102 cm; women >88 cm

Supplementary Table 4 Cross-sectional association between BMI and WC, and pre-frailty/frailty: The Tromsø Study 2015–2016

	Frailty status		Model 1	Model 2
	Robust (% (*n*))	Pre-frail/frail (% (*n*))	OR (95% CI)	OR (95% CI)
	70.5 (3179)	29.5 (1330)		
BMI, kg/m^2				
Underweight	0.5 (17)	1.4 (18)	2.93 (1.48–5.83)	2.32 (1.09–4.94)
Normal	30.0 (951)	24.5 (323)	Ref.	Ref.
Overweight	49.4 (1,566)	41.4 (547)	1.07 (0.91–1.26)	1.03 (0.86–1.23)
Obesity	20.1 (639)	32.7 (432)	2.14 (1.79–2.56)	1.88 (1.54–2.30)
WC, cm				
Normal	22.6 (716)	17.1 (225)	Ref.	Ref.
Moderately high	28.0 (888)	21.3 (281)	1.02 (0.83–1.25)*	1.01 (0.81–1.26)*
High	49.4 (1,569)	61.6 (812)	1.69 (1.42–2.01)*	1.45 (1.20–1.76)*

Model 1: minimally adjusted for age and sex (*excluding sex) at Tromsø7.
Model 2: adjusted for age, sex, educational level, smoking status, alcohol intake, comorbidities, social support, and self-perceived health (*excluding sex) at Tromsø7.
BMI, body mass index; CI, confidence interval; OR: odds ratio; WC, waist circumference.

Supplementary Table 5 Longitudinal association between BMI and WC, combined profiles and trajectories, and pre-frailty/frailty: The Tromsø Study 1994–2016

	Frailty status		Model 1	Model 2
	Robust (%) (n)	Pre-frail/frail (≥2) (%) (n)	OR (95% CI)	OR (95% CI)
BMI, kg/m²	n= 2925	n= 1125		
Underweight	0.4 (10)	0.7 (8)	2.28 (0.89–5.88)	1.37 (0.49–3.89)
Normal	48.0 (1404)	40.1 (451)	Ref.	Ref.
Overweight	43.0 (1259)	41.7 (469)	1.16 (0.99–1.36)	1.16 (0.99–1.36)
Obesity	8.6 (252)	17.5 (197)	2.38 (1.92–2.95)	2.31 (1.83–2.92)
WC, cm	n= 714	n = 387		
Normal	51.5 (368)	39.0 (151)	Ref.	Ref.
Moderately high	31.1 (222)	33.1 (128)	1.40 (1.05–1.87)*	1.50 (1.10–2.05)*
High	17.4 (124)	27.9 (108)	2.10 (1.52–2.89)*	2.19 (1.54–3.14)*
BMI and WC profile, baseline	n= 650	n = 347		
Normal BMI and normal WC	36.6 (238)	30.8 (107)	Ref.	Ref.
Normal BMI and moderately high/high WC	8.0 (52)	6.4 (22)	0.94 (0.54–1.63)*	0.92 (0.50–1.66)
Overweight and normal WC	15.4 (100)	9.2 (32)	0.73 (0.46– 1.15)*	0.74 (0.45– 1.20)
Overweight and moderately high/high WC	32.0 (208)	34.9 (121)	1.31 (0.95– 1.81)*	1.47 (1.04–2.08)
Obesity and moderately high/high WC	8.0 (52)	18.7 (65)	2.73 (1.77– 4.20)*	2.91 (1.83–4.65)
BMI trajectories	n= 653	n = 348		
Stable normal BMI	26.9 (176)	22.1 (77)	Ref.	Ref.
Stable overweight	46.6 (304)	41.1 (143)	1.16 (0.83–1.63)	1.14 (0.79–1.63)
Overweight to obese	22.4 (146)	25.9 (90)	1.53 (1.04–2.24)	1.55 (1.02–2.35)
Increasing obesity	4.1 (27)	10.9 (38)	3.35 (1.90–5.90)	3.17 (1.72–5.85)
WC trajectories (women)	n= 287	n = 172		
Normal to moderately high WC	25.5 (73)	20.4 (35)	Ref.	Ref.
Moderately high to high WC	50.5 (145)	38.9 (67)	0.98 (0.60–1.62)*	1.12 (0.65–1.93)*
Gradually increasing high WC	20.9 (60)	33.7 (58)	1.99 (1.15–3.43)*	2.02 (1.10–3.71)
Steeply increasing high WC	3.1 (9)	7.0 (12)	2.63 (1.01–6.86)*	3.30 (1.09–10.04)*
WC trajectories (men)	n= 366	n = 176		
Normal WC	21.6 (79)	17.6 (31)	Ref.	Ref.
Stable moderately high WC	41.5 (152)	36.4 (64)	1.09 (0.66–1.81)*	1.03 (0.60–1.76)*
Moderately high to high WC	32.2 (118)	29.6 (52)	1.17 (0.69–1.99)*	1.06 (0.60–1.87)*
Increasing high WC	4.6 (17)	16.5 (29)	4.51 (2.17–9.38)*	4.36 (1.94–9.80)*

[#] Analysis was restricted to individuals who were <60 years at Tromsø4
Model 1: adjusted for age and sex (*excluding sex) at baseline.
Model 2: adjusted for age, sex, educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level (*excluding sex) at baseline.
BMI, body mass index; CI, confidence interval; OR, odds ratio; WC, waist circumference.

Supplementary Table 6 Longitudinal association between BMI and WC, combined profiles and trajectories, and pre-frailty/frailty (frailty score ≥ 2): The Tromsø Study 1994–2016

	Frailty status		Model 1	Model 2
	Robust (%) (n)	Pre-frail/frail (≥2) (%) (n)	OR (95% CI)	OR (95% CI)
BMI, kg/m²	n= 2925	n= 199		
Underweight	0.4 (10)	0.5 (1)	1.45 (0.18–11.98)	0.95 (0.11–7.85)
Normal	48.0 (1404)	37.7 (75)	Ref.	Ref.
Overweight	43.0 (1259)	38.7 (77)	1.22 (0.87–1.71)	1.18 (0.82–1.71)
Obesity	8.6 (252)	23.1 (46)	3.47 (2.33–5.18)	3.27 (2.09–5.08)
WC, cm	n= 714	n = 88		
Normal	51.5 (368)	30.7 (27)	Ref.	Ref.
Moderately high	31.1 (222)	36.4 (32)	1.97 (1.15–3.38)*	1.98 (1.10–3.54)*
High	17.4 (124)	32.9 (29)	3.20 (1.82–5.64)*	3.18 (1.71–5.93)*
BMI and WC profile, baseline	n= 650	n = 81		
Normal BMI and normal WC	36.6 (238)	27.2 (22)	Ref.	Ref.
Normal BMI and moderately high/high WC	8.0 (52)	8.6 (7)	1.45 (0.59–3.59)	1.41 (0.52–3.86)
Overweight and normal WC	15.4 (100)	3.7 (3)	0.33 (0.09– 1.13)	0.37 (0.11– 1.31)
Overweight and moderately high/high WC	32.0 (208)	38.3 (31)	1.65 (0.92–2.95)	1.81 (0.97–3.38)
Obesity and moderately high/high WC	8.0 (52)	22.2 (18)	3.79 (1.89– 7.62)	3.66 (1.71–7.81)

#Analysis was restricted to individuals who were <60 years at Tromsø4 and had frailty score ≥2
Model 1: adjusted for age and sex (*excluding sex) at baseline.
Model 2: adjusted for age, sex, educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level (*excluding sex) at baseline.
BMI, body mass index; CI, confidence interval; OR, odds ratio; WC, waist circumference.

Supplementary Table 7 Longitudinal association between BMI and WC, and pre-frailty/frailty among individuals with information on all five frailty criteria: The Tromsø Study 1994–2016

	Frailty status		Model 1	Model 2
	Robust (%) (n)	Pre-frail/frail (%) (n)	OR (95% CI)	OR (95% CI)
	70.4% (2016)	29.6% (848)		
BMI, kg/m²				
Underweight	0.4 (8)	0.7 (6)	1.98 (0.67–5.84)	0.97 (0.28–3.23)
Normal	48.4 (976)	40.1 (340)	Ref.	Ref.
Overweight	42.8 (862)	42.9 (364)	1.19 (0.99–1.42)	1.18 (0.97–1.43)
Obesity	8.4 (170)	16.3 (168)	2.36 (1.82–3.05)	2.28 (1.72–3.01)
WC, cm	n = 600	n = 350		
Normal	53.3 (320)	40.9 (143)	Ref.	Ref.
Moderately high	31.3 (188)	34.0 (119)	1.40 (1.03–1.90)*	1.50 (1.08–2.08)*
High	15.3 (92)	25.1 (88)	2.15 (1.51–3.08)*	2.15 (1.46–3.18)*

Model 1: adjusted for age and sex (*excluding sex) at baseline.
Model 2: adjusted for age, sex, educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level (*excluding sex) at baseline.
BMI, body mass index; CI, confidence interval; OR, odds ratio; WC, waist circumference.

Supplementary Table 8 Longitudinal association between BMI and WC, and frailty components: The Tromsø Study 1994–2016

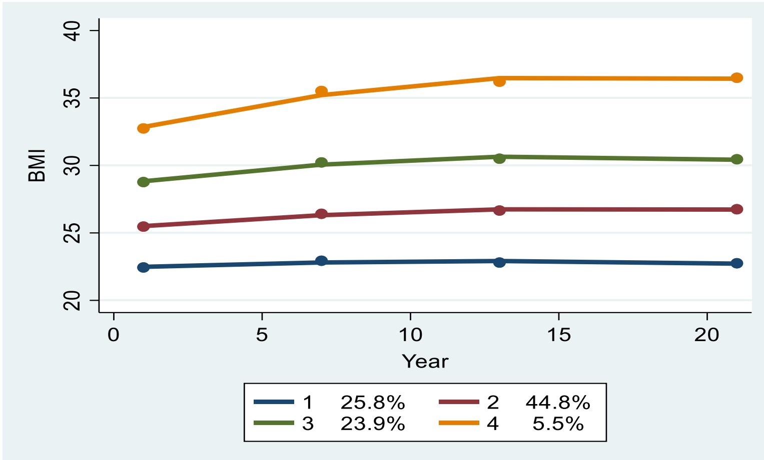
	Model 1 OR (95% CI)	Model 2 OR (95% CI)
Low grip strength		
BMI, kg/m^2		
Underweight	0.85 (0.11–6.63)	0.78 (0.10–6.17)
Normal	Ref.	Ref.
Overweight	1.45 (1.05–2.00)	1.34 (0.95–1.89)
Obesity	2.00 (1.31–3.05)	1.52 (0.95–2.43)
WC, cm		
Normal	Ref.	Ref.
Moderately high	0.99 (0.58–1.68)*	0.92 (0.51–1.65)*
High	1.40 (0.81–2.43)*	1.37 (0.75–2.50)*
Low walking speed		
BMI, kg/m^2		
Underweight	4.51 (1.20–16.95)	3.03 (0.64–14.35)
Normal	Ref.	Ref.
Overweight	1.63 (1.12–2.37)	1.67 (1.12–2.48)
Obesity	3.32 (2.13–5.16)	3.15 (1.96–5.07)
WC, cm		
Normal	Ref.	Ref.
Moderately high	2.24 (1.27–3.94)*	2.52 (1.38–4.63)*
High	2.65 (1.45–4.85)*	2.35 (1.19–5.63)*
Exhaustion		
BMI, kg/m^2		
Underweight	1.72 (0.22–13.18)	1.62 (0.20–13.24)
Normal	Ref.	Ref.
Overweight	1.11 (0.74–1.65)	1.06 (0.69–1.64)
Obesity	1.39 (0.793–2.42)	1.25 (0.69–2.27)
WC, cm		
Normal	Ref.	Ref.
Moderately high	1.67 (0.75–3.72)*	1.67 (0.72–3.89)*
High	1.74 (0.72–4.20)*	1.69 (0.66–4.29)*
Unintentional weight loss		
BMI, kg/m^2		
Underweight	2.84 (0.92–8.79)	2.15 (0.60–7.76)
Normal	Ref.	Ref.
Overweight	0.63 (0.49–0.82)	0.64 (0.49–0.85)
Obesity	0.68 (0.45–1.03)	0.70 (0.46–1.08)
WC, cm		
Normal	Ref.	Ref.
Moderately high	0.99 (0.64–1.55)*	1.10 (0.70–1.73)*
High	0.57 (0.57–1.03)*	0.56 (0.30–1.07)*
Low physical activity		
BMI, kg/m^2		
Underweight	–	–
Normal	Ref.	Ref.
Overweight	1.42 (1.16–1.74)	1.43 (1.15–1.79)
Obesity	3.62 (2.81–4.68)	3.71 (2.80–4.90)
WC, cm		
Normal	Ref.	Ref.
Moderately high	1.85 (1.24–2.78)*	1.71 (1.10–2.66)*
High	4.47 (2.97–6.72)*	4.94 (3.15–7.76)*

[#]Analysis was restricted to individuals who were <60 years at Tromsø4
Model 1: adjusted for age and sex (*excluding sex) at baseline.
Model 2: adjusted for age, sex, educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level (*excluding sex) at baseline.
BMI, body mass index; CI, confidence interval; OR, odds ratio; WC, waist circumference.

SUPPLEMENTARY FIGURES

Supplementary Figure 1 Trajectories of individuals with repeated body mass index measurements between Tromsø4 and Tromsø7: The Tromsø Study 1994–2016.

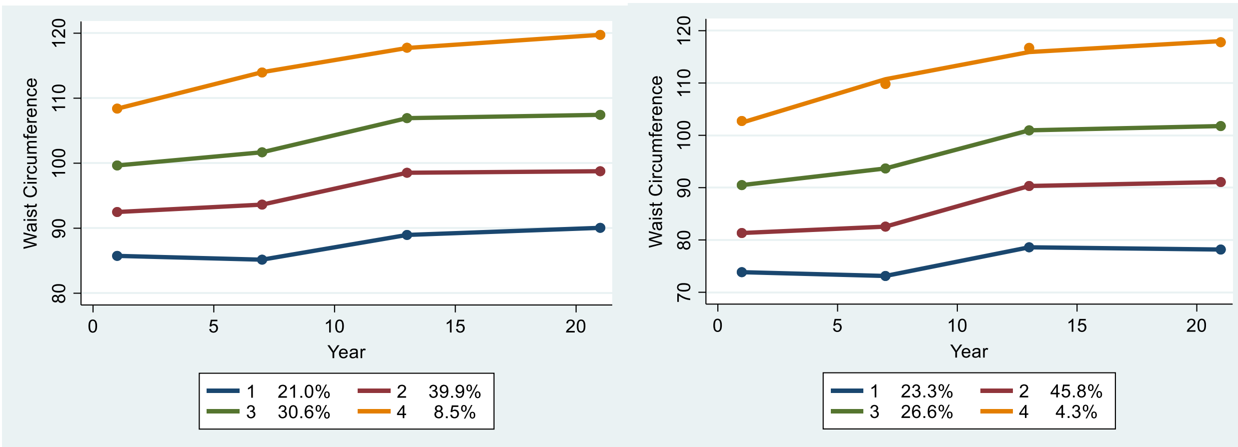
(n = 1,391)



Group 1	Stable normal weight	25.8%
Group2	Stable overweight	44.8%
Group 3	Overweight to obesity	23.9%
Group 4	Increasing obesity	5.5%

Supplementary Figure 2 Trajectories of individuals with repeated waist circumference measurements between Tromsø4 and Tromsø7: The Tromsø Study 1994–2016.

(Males: n = 731; females n = 660)



	Male	
Group 1	Stable normal WC	21.00%
Group 2	Stable moderately high WC	39.90%
Group 3	Moderately high to high WC	30.60%
Group 4	Increasing high WC	8.5 %

	Female	
Group 1	Stable normal WC	23.30%
Group 2	Moderately high to high WC	45.80%
Group 3	Gradually increasing high WC	26.60%
Group 4	Steeply increasing high WC	4.30%

Research checklist

	Item No	Content covered	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	√ (1-2)
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	√ (3)
Objectives	3	State specific objectives, including any pre-specified hypotheses	√ (3)
Methods			
Study design	4	Present key elements of study design early in the paper	√ (4)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	√ (4)
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed (*b*) Flow chart explaining inclusion and exclusion of partcipants	√ (4)
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	√ (4,5,6)
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	√ (4,5)
Bias	9	Describe any efforts to address potential sources of bias	√ (6)
Study size	10	Explain how the study size was arrived at	√ (4)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	√ (4,5,6)
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	√ (6)
Results			
Participants	13	(a) Information on participants	√ (4)
Descriptive data	14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	√ (7, 8)
Outcome data	15	Report numbers of outcome events or summary measures over time	√ (8-11)

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	√ (9-11)
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	√ (9-11)
Discussion			
Key results	18	Summarise key results with reference to study objectives	√ (11)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	√ (13)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	√ (11-14)
Generalisability	21	Discuss the generalisability (external validity) of the study results	√ (13-14)
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	√ (15)

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Body mass index, waist circumference and pre-frailty/frailty: The Tromsø study 1994−2016

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Keywords: body mass index, frailty, obesity, pre-frailty, waist circumference, prospective study

Abstract

Objective: This study investigated the association between obesity, assessed using body mass index (BMI) and waist circumference (WC), and pre-frailty/frailty among older adults over 21 years of follow-up.

Design: Prospective cohort study.

Setting: Population-based study among community-dwelling adults in Tromsø municipality, Norway.

Participants: 2340 women and 2169 men aged ≥45 years attending the Tromsø Study in 1994–1995 (Tromsø4) and 2015–2016 (Tromsø7), with additional BMI and WC measurements in 2001 (Tromsø5) and 2007–2008 (Tromsø6).

Primary outcome measure: Physical frailty was defined as the presence of 3 or more and pre-frailty as the presence of 1-2 of the five frailty components suggested by Fried et al.: low grip strength, slow walking speed, exhaustion, unintentional weight loss and low physical activity.

Results: Participants with baseline obesity (adjusted odds ratio [OR] 2.41, 95% confidence interval [CI] 1.93–3.02), assessed by BMI, were more likely to be pre-frail/frail than those with normal BMI. Participants with high (OR 2.14, 95% CI 1.59–2.87) or moderately high (OR 1.57, 95% CI 1.21–2.03) baseline WC were more likely to be pre-frail/frail than those with normal WC. Those at baseline with normal BMI but moderately high/high WC or overweight with normal WC had no significantly increased odds for pre-frailty/frailty. However, those with both obesity and moderately high/high WC had increased odds of pre-frailty/frailty. Higher odds of pre-frailty/frailty was observed among those in "overweight to obesity" or "increasing obesity" trajectories than those with stable normal BMI. Compared with participants in a stable normal WC trajectory, those with high WC throughout follow-up were more likely to be pre-frail/frail.

Conclusion: Both general and abdominal obesity, especially over time during adulthood, is associated with an increased risk of pre-frailty/frailty in later years. Thus maintaining normal BMI and WC throughout adult life is important.

Strengths and limitations of this study:

1. This study has a long follow-up period of 21 years.
2. This study takes into account changes in body mass index (BMI) and waist circumference (WC) occurring through the follow-up period.
3. Frailty status was defined using a slightly modified version of Fried's physical frailty criteria.
4. Frailty and pre-frailty were combined as one outcome.
5. Information on frailty was only available at follow-up.

Background

Frailty is a dynamic multifactorial geriatric syndrome characterised by physiological deterioration, increased vulnerability and decreased resilience toward external stressors.[1,2] Frailty is associated with an increased risk of adverse events such as falls, disability, hospitalisation, reduced quality of life, and mortality.[1,2] It is preceded by pre-frailty, a multidimensional, transitional risk state.[3,4] Fried's frailty phenotype identifies pre-frailty as the presence of one or two and frailty as three or more of the five criteria: unintentional weight loss, self-reported exhaustion, weakness, slow walking speed, and low physical activity.[5] The prevalence of frailty and pre-frailty, defined using Fried's physical frailty measure,[5] among community-dwelling people aged ≥50 years across 62 countries, has been estimated to be 12% and 46%, respectively.[6]

Rapid population ageing has become a global phenomenon.[7] Ageing is typically associated with changes in body composition, such as decreased muscle mass and redistribution of total and regional fat.[8–10] Underweight older adults with minimal reserve capacity are at risk of adverse health outcomes[5,11], and unintentional weight loss is commonly acknowledged as a significant frailty indicator.[5] However, a growing body of evidence also suggests a positive association between obesity among older adults and the risk of frailty.[10,12–16] Obesity aggravates the age-related decline in muscle strength, aerobic capacity, and physical functionality, thus worsening health and well-being.[10,11,14,17,18] It is also closely associated with metabolic disorders, inflammaging and oxidative stress, all of which have been suggested to contribute to the risk of frailty.[14,19]

Anthropometric measures, including body mass index (BMI) and waist circumference (WC), are simple, cost-effective tools that reflect an individual's body composition and nutritional status. They are one of the widely used nutritional items for detecting frailty.[20] BMI indicates general obesity, while WC indicates abdominal obesity. When used together, they effectively assess obesity-related risks at the population level.[21–23] Some studies have detected a U-shaped association between BMI and frailty.[13,15,24] Midlife overweight and obesity, assessed by BMI, have been associated with the risk of pre-frailty and frailty in older age.[25,26] Similarly, a positive association between high WC and frailty among older adults has been observed in some studies.[9,16,27–29] These findings are even more relevant in the present context, where obesity prevalence is increasing across all age groups, posing a global public health challenge.[30]

Though the evidence is expanding, there have been limited longitudinal studies exploring and comparing the relationship of both BMI and WC with the risk of developing pre-frailty and frailty over a long follow-up period.[29] Few have explored changes in BMI[31,32] and its association with frailty, while studies that consider changes in WC in association with the development of frailty seem to be lacking. Therefore, the present study aimed to investigate the association of BMI and WC, separately and concurrently, with the risk of pre-frailty/frailty after 21 years of follow-up. Additionally, this study assessed changes in BMI and WC through the follow-up period and their association with pre-frailty/frailty.

Methods

The Tromsø study

This study uses data from the Tromsø study, an ongoing population-based study in the Tromsø municipality, Norway, consisting of seven surveys: Tromsø1 (1974), Tromsø2 (1979–1980), Tromsø3 (1986–1987), Tromsø4 (1994–1995), Tromsø5 (2001), Tromsø6 (2007–2008), and Tromsø7 (2015–2016). More than 45,000 women and men have participated in at least one of the surveys.[33] The earlier surveys (Tromsø1-Tromsø3) did not include WC measurements. Therefore, the present study uses data from Tromsø4 (baseline) to Tromsø7 (follow-up). Tromsø4 included 27,158 participants aged 25–97 years, Tromsø5, 8,130 participants aged 30–89 years, Tromsø6, 12,984 participants aged 30–87 years, and Tromsø7, 21,083 participants aged 40–99 years. The detailed information on the recruitment and the attendance of the participants has been described elsewhere.[33]

Study sample

The present study included Tromsø4 participants aged ≥45 years with valid information on BMI who also attended Tromsø7, i.e., 21 years of follow-up (n = 4,809). Participants with missing information on three or more frailty indicators in Tromsø7 were excluded (Figure 1). Our primary analytical sample had 4,509 participants. Out of these, 1,534 participants had information on WC at Tromsø4, and 1,391 had repeated measurements on both BMI and WC between Tromsø4 and Tromsø7.

Exposure

Bodyweight in kilograms and height in metres were measured wearing light clothes and no footwear. WC was measured using tape to the nearest centimetre at the umbilical level. All measurements were performed by trained personnel. BMI was calculated as the weight divided by the square of the height (kg/m^2) and categorised as underweight (<18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), and obesity (≥30.0 kg/m^2) according to the World Health Organization (WHO) criteria.[34] WC was categorised as normal (men ≤94 cm, women ≤80 cm), moderately high (men 95–102 cm, women 81–88 cm), and high (men>102 cm, women >88 cm) according to WHO.[35]

Frailty assessment

A modified version of Fried et al.'s frailty phenotype[5] was used to operationalise frailty in Tromsø7. Frailty was not operationalised at baseline as complete information on frailty indicators was unavailable. Five indicators were assessed at follow-up (Supplementary Table 1):

1. Unintentional weight loss: Self-reported involuntary weight loss during the last six months.[36]
2. Exhaustion: Response "pretty much" or "very much" to the question: "During the last week, have you experienced that everything is a struggle?" from the Hopkins' Symptom Checklist-10.[37]
3. Walking speed: Short Physical Performance Battery test, [38,39] where the fastest time out of two walks was selected and converted to seconds per 15 feet from seconds per 4 meters. Sex- and height-adjusted cut-offs, according to Fried et al.,[5] were used to identify participants with a low walking speed.
4. Weakness: Grip strength was measured using a newly calibrated Jamar+ Digital Dynamometer (Patterson Medical, Warrenville, IL, USA) following the Southampton protocol procedures.[40] Sex- and BMI-specific cut-offs suggested by Fried et al. [5] were used to identify participants with low grip strength.
5. Low physical activity: Response "Reading, watching TV/screen or other sedentary activity" to the question: "Describe your exercise and physical exertion in leisure time over the last year" from the Saltin–Grimby Physical Activity Level Scale for leisure-time physical activity.[41]

Participants were categorised as robust (0), pre-frail (1-2) and frail (≥3) based on the number of frailty indicators present.

Covariates

The potential covariates in this study were selected based on the existing knowledge and literature on frailty status. Sociodemographic characteristics included age, sex, educational level [primary/partly secondary education (up to 10 years of schooling), upper secondary education (minimum of 3 years), college/university short (<4 years), and college/university long (≥4 years)], and marital/cohabitation status (married/cohabiting or single/not cohabiting with a partner). Self-reported smoking status was categorised as current, former, or never smoker. Self-reported alcohol intake level was categorised as never-drinker, infrequent drinker (<2–4 times/month), and frequent drinker (>2–3 times/week). Comorbidity was defined using Charlson's comorbidity index[42] without weighting of the diseases. It was categorised as "no comorbidity" and "comorbidity" based on the self-reported presence of coronary heart disease (angina pectoris/myocardial infarction), stroke, diabetes, cancer, pulmonary disease (asthma/chronic bronchitis/emphysema), and peptic ulcer. Social support was categorised as self-reported "not enough good friends" or "enough good friends."

Self-perceived health status was categorised as "poor" or "good." Baseline physical activity level was categorised as no/low physical activity (0 hours/week spent in hard physical activity or ≤2 hours/week spent in light physical activity) and high physical activity (≥1 hour/week in hard physical activity or ≥3 hours/week in light physical activity).

Statistical analysis

The sociodemographic and lifestyle factors at baseline across robust and pre-frail/frail groups were described using mean and standard deviation for continuous variables and proportion and count for categorical variables. The differences between the two groups were tested using the student's *t*-test for continuous variables and the chi-square test for categorical variables.

Multivariable logistic regression analysis was used to assess the effect of BMI and WC on pre-frailty/frailty at follow-up. Five different longitudinal associations were assessed: baseline BMI and pre-frailty/frailty; baseline WC and pre-frailty/frailty; joint BMI and WC profile at baseline and pre-frailty/frailty; BMI trajectories and pre-frailty/frailty; WC trajectories and pre-frailty/frailty. The models were minimally adjusted for age and sex (Model 1) and further adjusted for educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level at baseline (Model 2). The adjustment variables were selected using a stepwise backward regression procedure. No significant collinearity or interaction was detected between covariates in the model.

Group-based trajectory modelling (GBTM) was conducted among 1,391 participants to assess changes in the BMI and WC throughout the 21-year follow-up period, with measurements on both BMI and WC available at Tromsø4, Tromsø5, Tromsø6 and Tromsø7. GBTM, also known as latent class growth analysis, is a semi-parametric technique that identifies distinct subgroups of individuals following a similar pattern of change over time on a given variable, using finite mixtures of defined probability distributions.[43] Different models with varying numbers of trajectory groups, varying functional forms and orders were compared. The most appropriate model was selected based on the Bayesian Information Criterion[44] and then introduced into longitudinal multivariable logistic regression models. The distinct BMI and WC trajectories were named based on their observed pattern. The WC trajectories were sex-stratified due to varying cut-off levels for men and women.

A new variable with five distinct strata (normal BMI and normal WC; normal BMI and moderately high/high WC; overweight and low WC; overweight and moderately high/high WC; obesity and moderately high/high WC) was formed by combining different categories of BMI and WC. They were then introduced into the multivariable models to assess the concurrent effects of BMI and WC on frailty status. While

forming the new joint variable, the underweight group was removed because of low prevalence (<1%), and moderately high and high WC groups were combined because of their low sample size when stratified.

Additional supplementary analyses were carried out. The cross-sectional association between BMI and WC level and frailty status at Tromsø7 was assessed. Since pre-frailty/frailty could not be assessed at baseline, the primary longitudinal analyses were repeated in a sub-population (*n*= 4,050), excluding participants aged 60 years and older at Tromsø4 who might have had an increased probability of being pre-frail/frail at that time point. The majority of the participants in the pre-frail/frail group had a frailty score of 1. In order to account for potential misclassification, analyses were performed on a further restricted sub-sample with a frailty score ≥2 at Tromsø7 (*n*= 3,124). The primary longitudinal analyses were also repeated among the subgroup of participants with non-missing information on all five frailty components (*n* = 2,864), and the association of obesity with each frailty component were assessed.

All the statistical analyses were conducted using STATA 16.[45] Statistical significance was set at $P < 0.05$. The results are expressed as adjusted odds ratios (ORs) with 95% confidence intervals (CIs).

Patient and public involvement

Patients and the public were not involved in this research's design, conduct, reporting, or dissemination plans.

Results

Study population

The mean age at baseline was 51.6 years, and the participants were followed up for 21 years. 28.4% of the participants were pre-frail, 1.1% were frail, and 70.5% were robust at follow-up (Table 1). In total, 50.6% of the robust group and 55.0% of the pre-frail/frail group were women. Most robust and pre-frail/frail participants were either married or cohabiting (84.3% and 80.3%) and reported having enough good friends (83.1% and 80.5%) at baseline. All the baseline characteristics, except comorbidity, were significantly different in the robust and the pre-frail/frail groups (Table 1).

When assessed at follow-up, all the sociodemographic, lifestyle and disease-related factors were significantly associated with pre-frailty/frailty (Supplementary Table 2). When the eligible participants lost to follow-up (*n* = 8,649) were compared with the attendees, they were found to be older (mean age 63.2 years) with a less healthy lifestyle and higher comorbidities (Supplementary Table 3).

BMI and WC

At baseline, the proportion of individuals with underweight was low (<1%) (Table 2). The proportion of individuals with normal BMI was higher among the robust group than the pre-frail/frail group (47.6% versus 39.3%), whereas the proportion of individuals with obesity was higher among the pre-frail/frail group (17.1% versus 8.4%). The robust group had a higher proportion of individuals with normal WC than the pre-frail/frail group (51.5% versus 37.3%), whereas the pre-frail/frail group had a higher proportion of individuals with high WC (27.7% versus 17.4%). A similar distribution of different BMI and WC categories across robust and pre-frail/frail groups was observed at follow-up (Supplementary Table 2). Both robust and pre-frail/frail groups at follow-up had an increased proportion of individuals with obesity and high WC compared with baseline (Table 2; Supplementary Table 2).

Table 1 Baseline characteristics of participants by frailty status at follow-up: The Tromsø Study 1994–2016

	Frailty status		
	Robust (% (*n*)) 70.5 (3,179)	**Pre-frail/frail (% (*n*)) 29.5 (1,330)**	***P* value**
Age in years, mean (SD)	51.1 (5.1)	52.8 (5.9)	0.000[a]
Women	50.6 (1,608)	55.0 (732)	0.006
Smoking status			
Current smokers	27.0 (858)	33.7 (448)	
Former smokers	36.1 (1,149)	34.0 (452)	0.001
Never	36.9 (1,172)	32.3 (430)	
High physical activity level	69.5 (2,210)	56.9 (756)	0.001
Married or cohabiting	84.3 (2,679)	80.3 (1,068)	0.001
Self-perceived health – good	75.4 (2,394)	61.5 (818)	<0.001
Social support – enough good friends	83.1 (2,404)	80.5 (976)	0.041
Educational level			
Primary/Partly secondary	32.8 (1,041)	42.4 (562)	
Upper secondary	34.3 (1,085)	34.2 (453)	<0.001
College/University short	16.5 (524)	12.8 (169)	
College/University long	16.4 (520)	10.6 (141)	
Alcohol intake			
Never/Abstaining	9.0 (286)	11.9 (158)	
Infrequent drinker	76.2 (2,419)	76.6 (1,015)	<0.001
Frequent drinker	14.8 (468)	11.5 (152)	
Prevalent diseases			
Pulmonary disease[b]	8.6 (272)	9.5 (126)	0.323
Coronary heart disease[c]	2.3 (73)	4.5 (59)	<0.001
Diabetes	0.4 (12)	0.6 (8)	0.300
Cancer	2.8 (79)	3.5 (42)	0.210
Stroke	0.6 (19)	0.8 (11)	0.386
Peptic ulcer	7.0 (197)	8.9 (105)	0.033
Comorbidity	1.9 (59)	2.7 (36)	0.070

Values are percentages (numbers); *P* value: χ^2 test for categorical variables; *P* value: [a]Student's t-test; [b]including asthma/chronic bronchitis/emphysema; [c]including angina pectoris/myocardial infarction.

When BMI and WC level was assessed jointly at baseline (Table 3), the robust group had a higher proportion of individuals with both BMI and WC in the normal range than the pre-frail/frail group (36.1% versus 29.1%). The proportion of individuals with both obesity and moderately high/ high WC was higher among the pre-frail/frail group (16.9% versus 7.4%).

The GBTM resulted in four distinct trajectories of BMI (n = 1391): stable normal BMI (25.8%), stable overweight (44.8%), overweight to obesity (23.9%), and increasing obesity (5.5%) (Supplementary Figure 1). The increasing obesity trajectory included individuals with BMI ≥30 kg/m^2 at baseline, which kept increasing to a higher obesity level, i.e., BMI ≥35 kg/m^2. Four distinct WC trajectories were identified for both women (n = 660) and men (n = 731) (Supplementary Figure 2). The WC trajectories for women were: stable normal WC (23.3%), moderately high to high WC (45.8%), gradually increasing high WC (26.6%), and steeply increasing high WC (4.3%). The WC trajectories for men were: stable normal WC (21.0%), stable moderately high WC (39.9%), moderately high to high WC (30.6%), and increasing high WC (8.5%).

BMI, WC, and pre-frailty/frailty

Individuals who had obesity (OR 2.41, 95% CI 1.93–3.02) or overweight (OR 1.19, 95% CI 1.02–1.39) at baseline had significantly higher odds of becoming pre-frail/frail at follow-up compared with individuals with normal BMI (Model 2, Table 2). No statistically significant association was detected between underweight group and the odds of pre-frailty/frailty; however, the number of underweight individuals was insufficient to reach any conclusion. Participants with moderately high WC (OR 1.57, 95% CI 1.21–2.03) or high WC (OR 2.16, 95% CI 1.59–2.87) at baseline had higher odds of becoming pre-frail/frail at follow-up compared to individuals with a normal WC (Model 2, Table 2).

The supplementary cross-sectional analysis (Supplementary Table 4) indicated a significant association between obesity and pre-frailty/frailty among older adults (OR 1.88, 95% CI 1.54–2.30), whereas no association was detected between overweight and pre-frailty/frailty. As for WC, only high WC was associated with increased odds of pre-frailty/frailty (OR 1.45, 95% CI 1.20–1.76) in the cross-sectional analysis.

Table 2 Longitudinal association between BMI and WC, and pre-frailty/frailty: The Tromsø Study 1994–2016

	Frailty status			
	Robust (% (n))	**Pre-frail/frail (% (n))**	**Model 1 OR (95% CI)**	**Model 2 OR (95% CI)**
	70.5 (3179)	29.5 (1330)		
BMI, kg/m^2				
Underweight	0.3 (11)	0.7 (9)	2.15 (0.88–5.29)	1.32 (0.49–3.54)

Normal	47.6 (1,513)	39.3 (522)	Ref.	Ref.
Overweight	43.7 (1,388)	43.0 (572)	1.18 (1.02–1.36)	1.19 (1.02–1.39)
Obesity	8.4 (267)	17.0 (227)	2.42 (1.98–2.98)	2.41 (1.93–3.02)
WC, cm	*n* = 952	*n* = 582		
Normal	51.5 (490)	37.3 (217)	Ref.	Ref.
Moderately high	31.1 (296)	35.0 (204)	1.54 (1.21–1.96)*	1.57 (1.21–2.03)*
High	17.4 (166)	27.7 (161)	2.16 (1.65–2.83)*	2.14 (1.59–2.87)*

Model 1: adjusted for age and sex (*excluding sex) at baseline.
Model 2: adjusted for age, sex, educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level (*excluding sex) at baseline.
BMI, body mass index; CI, confidence interval; OR: odds ratio; WC, waist circumference.

BMI categories
Underweight: <18.5 kg/m^2
Normal: 18.5–24.9 kg/m^2
Overweight: 25.0–29.9 kg/m^2
Obesity: ≥30 kg/m^2

WC categories
Normal: men ≤94 cm; women ≤80 cm
Moderately high: men 95–102 cm; women 81–88 cm
High: men >102 cm; women >88 cm

The longitudinal model that included joint BMI and WC profile at baseline showed that participants who had overweight with moderately high/high WC (OR 1.48, 95% CI 1.11–1.98) or participants who had obesity with moderately high/high WC (OR 3.11, 95% CI 2.07–4.70) had higher odds of being pre-frail/frail compared with participants with normal BMI and normal WC (Model 2, Table 3). No significant association with pre-frailty/frailty was detected among participants who had normal BMI with moderately high/high WC or overweight with normal WC at baseline.

The sensitivity analyses restricted to participants with baseline age <60 years (Supplementary Table 5) and further restricted to those with a frailty score ≥2 at follow-up (Supplementary Table 6) confirmed the higher odds of pre-frailty/frailty among participants with baseline obesity and/or moderately high/ high WC. However, no significant association was detected between participants in overweight category and pre-frailty/frailty. The sensitivity analysis among participants with complete information on all five frailty components (Supplementary Table 7) also generated similar results.

Table 3 Association between combined BMI and WC profiles, and pre-frailty/frailty: The Tromsø Study 1994–2016

Longitudinal	Frailty status: Robust (% (*n*))	Frailty status: Pre-frail/frail (% (*n*))	Model 1 OR (95% CI)	Model 2 OR (95% CI)
BMI and WC profile, baseline	62.8 (870)	37.2 (515)		
Normal BMI and normal WC	36.1 (314)	29.1 (150)	Ref.	Ref.
Normal BMI and moderately high/high WC	8.4 (73)	8.0 (41)	1.13 (0.73–1.74)	1.01 (0.63–1.61)
Overweight and normal WC	15.9 (139)	9.5 (49)	0.74 (0.50–1.08)	0.79 (0.53–1.19)
Overweight and moderately high/high WC	32.2 (280)	36.5 (188)	1.40 (1.07–1.84)	1.48 (1.11–1.98)
Obesity and moderately high/high WC	7.4 (64)	16.9 (87)	2.86 (1.96–4.18)	3.11 (2.07–4.70)

Model 1: adjusted for age at baseline.
Model 2: adjusted for age, educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level at baseline.

BMI, body mass index; CI, confidence interval; OR: odds ratio; WC, waist circumference.

The model with BMI trajectories (Model 2, Table 4) indicated higher odds of pre-frailty/frailty among participants in the overweight to obesity trajectory (OR 1.67, 95% CI 1.19–2.35) or those in the constantly increasing obesity trajectory (OR 3.12, 95% CI 1.80–5.41), compared with those in the stable normal BMI trajectory. Contrarily, there was no significant association in the stable overweight category. The model with WC trajectories (Model 2, Table 4) showed that women in the gradually increasing high WC trajectory (OR 2.17, 95% CI 1.32–3.59) or the steeply increasing high WC trajectory (OR 4.09, 95% CI 1.54–10.90) had higher odds of being pre-frail/frail compared with women in the normal WC trajectory. Similarly, men in the increasing high WC trajectory (OR 3.36, 95% CI 1.71–6.59) had higher odds of pre-frailty/frailty compared with men in the normal WC trajectory. The same trend in the association between different BMI and WC trajectories and pre-frailty/frailty was observed in sensitivity analyses restricted to participants with baseline age <60 years (Supplementary Table 5).

When the association was assessed separately for each frailty component (Supplementary Table 8), overweight or obesity at baseline was associated with higher odds of slow walking speed, low physical activity and low grip strength at follow-up. However, the association between BMI and grip strength was no longer significant in the fully adjusted model. Moderately high or high WC at baseline was associated with higher odds of slow walking speed and low physical activity.

Table 4 Association between BMI and WC trajectories and pre-frailty/frailty: The Tromsø study 1994–2016

	Frailty status		Model 1	Model 2
	Robust (% (*n*))	Pre-frail/frail (% (*n*))	OR (95% CI)	OR (95% CI)
	62.8 (874)	37.2 (517)		
BMI trajectories				
Stable normal BMI	27.8 (243)	22.4 (116)	Ref.	Ref.
Stable overweight	46.6 (407)	42.4 (219)	1.20 (0.91–1.59)	1.21 (0.90–1.62)
Overweight to obese	21.8 (191)	26.5 (137)	1.62 (1.18–2.22)	1.67 (1.19–2.35)
Increasing obesity	3.8 (33)	8.7 (45)	3.07 (1.85–5.09)	3.12 (1.80–5.41)
	59.4 (392)	40.6 (268)		
WC trajectories (women)				
Stable normal WC	26.3 (103)	17.5 (47)	Ref.	Ref.
Moderately high to high WC	49.7 (195)	42.5 (114)	1.27 (0.84–1.94)*	1.30 (0.83–2.05)*
Gradually increasing high WC	20.9 (82)	33.6 (90)	2.34 (1.47–3.70)*	2.17 (1.32–3.59)*
Steeply increasing high WC	3.1 (13)	6.3 (17)	3.04 (1.34–6.90)*	4.09 (1.54–10.90)*
	65.9 (482)	34.1 (249)		
WC trajectories (men)				
Stable normal WC	22.4 (108)	18.1 (45)	Ref.	Ref.
Stable moderately high WC	41.1 (198)	38.5 (96)	1.18 (0.77–1.80)*	1.12 (0.72–1.76)*
Moderately high to high WC	31.5 (152)	28.9 (72)	1.18 (0.75–1.85)*	1.12 (0.69–1.79)*
Increasing high WC	5.0 (24)	14.5 (36)	3.73 (1.99–6.97)*	3.36 (1.71–6.59)*

Model 1: adjusted for age and sex at baseline (*adjusted for age only).

Model 2: adjusted for age, sex, educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level (*excluding sex) at baseline.
BMI, body mass index; CI, confidence interval; OR: odds ratio; WC, waist circumference.

Discussion

The present study followed 4,509 community-dwelling participants from the population-based Tromsø Study from 1994 to 2016 to examine the association between general and abdominal obesity and the risk of frailty. This study suggests an increased likelihood of pre-frailty/frailty among those with baseline obesity. Increased likelihood of pre-frailty/frailty was also observed among those with high or moderately high WC at baseline. When assessed jointly, participants with both obesity and moderately high/high WC at baseline had increased odds of being pre-frail/frail compared to those with BMI and WC in the normal range. Participants in the "overweight to obesity" or the "increasing obesity" trajectories had increased odds of pre-frailty/frailty compared with those in the stable normal BMI trajectory. Additionally, participants with a high WC at baseline, whose WC gradually or steeply increased throughout the follow-up period, had increased odds of being pre-frail/frail compared with those in a stable normal WC trajectory.

Our conclusions align with the findings from two previous longitudinal studies with a similar follow-up period (26 and 22 years) that reported a significant positive association between midlife overweight or obesity and the development of pre-frailty and frailty in later life.[25,26] However, we should be cautious while interpreting the association between baseline overweight BMI and pre-frailty/frailty. In our study, this association was not significant in the sensitivity analyses where we excluded participants aged 60 years and older at baseline. A prospective study with a follow-up period of 3.5 years observed a significantly increased risk of frailty among underweight women and women with overweight and obesity.[24] No significant association between baseline underweight status and risk of pre-frailty/frailty was detected in our study. However, the number of underweight individuals in our study was too low, resulting in a low statistical power to reach any conclusion. In terms of WC and frailty status, similar to our results, a positive association between higher WC and frailty among older adults was reported by a 3.5-year follow-up study from two prospective Spanish cohorts.[29] A positive association between high WC and frailty was observed in a few other studies;[9,16,27] however, they were cross-sectional and used slightly different cut-offs to categorise WC. We identified BMI and WC trajectories to account for the dynamic change in the adiposity level that might occur during adulthood. In line with our findings regarding BMI trajectories, comparable trajectories and observations about a higher risk of pre-frailty and frailty among those with increasing BMI were observed in a 26-year follow-up study.[32] A large study that followed adults aged ≥51 years for ten years reported a higher incidence of frailty among weight gain class, weight loss class, and consistent obesity class.[31] Literature on long-term changes in WC and its association with frailty seems lacking. Few epidemiological studies have explored the combined effect of BMI and WC on frailty among older adults. Two studies conducted among adults aged ≥65 years in Portugal[46] and ≥60 years in Spain[29] observed a positive association between frailty and adiposity only when the individuals had both a high WC and a high BMI. It aligns with our results to a certain extent, as we observed an increased likelihood of pre-frailty/frailty among individuals with both obesity and moderately high/high WC at baseline. We also observed higher odds of pre-frailty/frailty among those who had overweight with a moderately high/high WC at baseline. However, this association was not significant in the sensitivity analyses where we excluded participants aged 60 years and older at baseline. On the contrary, high WC was reported to be associated with frailty regardless of their BMI categories by two cross-sectional studies conducted among community-dwelling adults aged ≥65 years in China[27] and England,[15] indicating WC to be better linked with frailty. Notably, participants who had normal BMI with moderately high/high WC or those who had overweight with normal WC did not have significantly increased odds of pre-frailty/frailty in our study. This finding indicates the importance of considering both BMI and WC to identify the risk of frailty.

There are different mechanisms through which obesity might contribute to pre-frailty/frailty. Increased adiposity leads to increased secretion of pro-inflammatory adipokines, thus contributing to inflammation,[14,19] which is also associated with frailty among older adults.[47] Obesity leads to increased fat mass and increased lipid infiltration in muscle fibres resulting in reduced muscle strength and function.[14,48] When coupled with an age-related decline in muscle mass and strength, it causes "sarcopenic obesity", which is linked to an increased risk of frailty and disability.[19,49,50] Grip strength, often used as a proxy for muscle strength in older adults, was found to be associated with baseline overweight and obesity assessed using BMI in our study. However, the association was no longer significant when further adjusted for potential covariates. Slow walking speed and low physical activity, which often represent lower physical functioning at an older age, were significantly associated with baseline BMI and WC. The primary strength of this study is its prospective design with a long follow-up period of two decades. However, several changes in participant's lifestyle, diet, habits, and physical and psycho-social environments might have occurred during this period. We could not account for these factors, which potentially impacted the development of pre-frailty/frailty. So, the result of this study should be cautiously interpreted in light of these contextual issues. We used BMI and WC to define general and abdominal obesity. BMI is often criticised for its inability to provide information on fat distribution,[22] while WC is criticised for its limitation in distinguishing between visceral and subcutaneous fat.[51] However, they are effective in assessing obesity-related risks at the population level.[21,22] A study among Tromsø7 participants aged ≥40 years found a strong correlation between BMI and visceral adipose tissue (VAT) mass and WC and VAT mass. It also concluded them to be a satisfactory substitute to identify cardiometabolic risk.[23] Further, they are simple to measure, easy to replicate, and widely used in routine health assessments, thus, helping identify individuals at risk of frailty to provide timely interventions. The repeated measures on BMI and WC allowed us to account for changes in participants' obesity status through the follow-up period and gain a comprehensive understanding of the long-term effects of these exposures on the risk of frailty in later life. However, we could not account for the development and change in frailty status that might have occurred over time as repeated measures on frailty were unavailable. Our outcome was physical frailty, assessed using Fried et al.'s frailty phenotype definition.[5] Though widely used,[52] it defines frailty from the unidimensional perspective of reduced physical functioning and declining physiological reserves. In the context where frailty is being recognised as a multidimensional construct encompassing not just physical but also cognitive, social and psychological dimensions [53], the scope of our results focusing just on physical aspects of frailty might be limited. This study's objectively measured physical frailty components (low grip strength and low walking speed) aligned with Fried's definition; however, the questionnaires for self-reported components (exhaustion, low physical activity and unintentional weight loss) varied slightly. Each frailty indicator we utilised has been validated in different research contexts.[36–38,41] The self-reported frailty components are nevertheless prone to information bias. A systematic review that investigated 262 physical frailty phenotypes acknowledged that modifications in the definition of frailty phenotype are common and have an important impact on the classification and predictive ability of the definition.[54] A fair agreement has been reported between Fried's definition and the completely questionnaire-based physical frailty definition.[55,56]

The main limitation of our study is the selection bias resulting from differential loss to follow-up. Those lost to follow-up were comparatively older and had a higher proportion of general and abdominal obesity and other potential risk factors for frailty. This might have led to a lower prevalence of frailty in Tromsø7. In total, 1.1% of the participants aged ≥66 years at Tromsø7 were frail, and 28.4% were pre-frail which is much lower than the pooled prevalence estimates provided by O'Caoimh et al.[6] It aligns with the findings from a study where the grip strengths of Tromsø7 participants and Russian Know Your Heart study participants aged 40-69 years were compared. The average Norwegian participant had a mean grip strength comparable to a seven-year younger Russian counterpart.[57] This indicates that the nordic population might be comparatively healthier,[58] thus limiting the generalisability of our findings to other populations across the globe. Only a sub-sample of our study population had information on both BMI and WC, and an even lower number had repeated measurements available for both exposures. Therefore, the models including both BMI and WC might have low statistical power, particularly when considering the repeated measures. Information on frailty measures was not available at baseline. However, most participants were in their mid-life (median age 50) at baseline, lowering their likelihood of having frailty components. The sensitivity analyses, where we excluded participants aged ≥60 years from baseline as a proxy for exclusion of pre-frail/frail individuals, showed a similar trend in the association between baseline obesity, assessed using BMI and WC, and pre-frailty/frailty at an older age. We adjusted for several confounding factors; however, the potential for residual confounding remains. Most covariates in our study, including comorbidity, were self-reported.

We combined pre-frailty and frailty as a single outcome because of the low frailty prevalence in this study. The pre-frail/frail population in this study is primarily pre-frail with a frailty score of 1, half of which were the ones with low physical activity. So, misclassification of comparatively healthier but less active participants with severely pre-frail/frail participants might have occurred. The sensitivity analyses on participants with ≥2 frailty score, which mostly supported results from the primary analysis, addressed this issue to some extent. It would have been informative to assess the association with pre-frailty and frailty separately. Nevertheless, understanding factors associated with pre-frailty is highly relevant because pre-frailty is gaining broader interest as an ideal opportunity for administering timely intervention to delay or reverse frailty and the associated adverse outcomes.[59] Of note, as our outcome pre-frailty/frailty is common, the OR estimates obtained might slightly overestimate the relative risk, and caution should be applied while interpreting it as a risk.

In the context where the population is rapidly ageing and the obesity epidemic is rising, growing evidence recognises the subgroup of "fat and frail" older individuals in contrast to viewing frailty only as a wasting disorder.[12,15,26] In this study, participants with both high BMI and high WC, i.e., general and abdominal obesity, especially for a long duration throughout their adulthood, were observed to have an increased likelihood of pre-frailty/frailty. It highlights the importance of routinely assessing and maintaining optimal BMI and WC throughout adulthood to lower the risk of frailty in older age.

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Competing Interest

None declared.

Ethical approval

The Tromsø Study was approved by the Regional Committee of Medical and Health Research Ethics (REK) North and the Norwegian Data Protection Authority. Approvals from REK (ref. 2021/234146) and the Norwegian Centre for Research Data (NSD) (ref. 364331) were obtained for this particular study.

Contributions

SU was responsible for conceptualisation, data acquisition, analysis, interpretation, writing original draft, review and editing; LFA was responsible for conceptualisation, funding acquisition, supervision, writing critical review and editing; LAH was responsible for data acquisition for the Tromsø Study, constant coordination, writing critical review and editing; AH was responsible for conceptualisation, funding acquisition, data acquisition, supervision, writing critical review and editing.

Data availability statement

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 can be made available from the Tromsø Study upon application to 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 <mailto:tromsous@uit.no>.

Patient consent for publication

Not required

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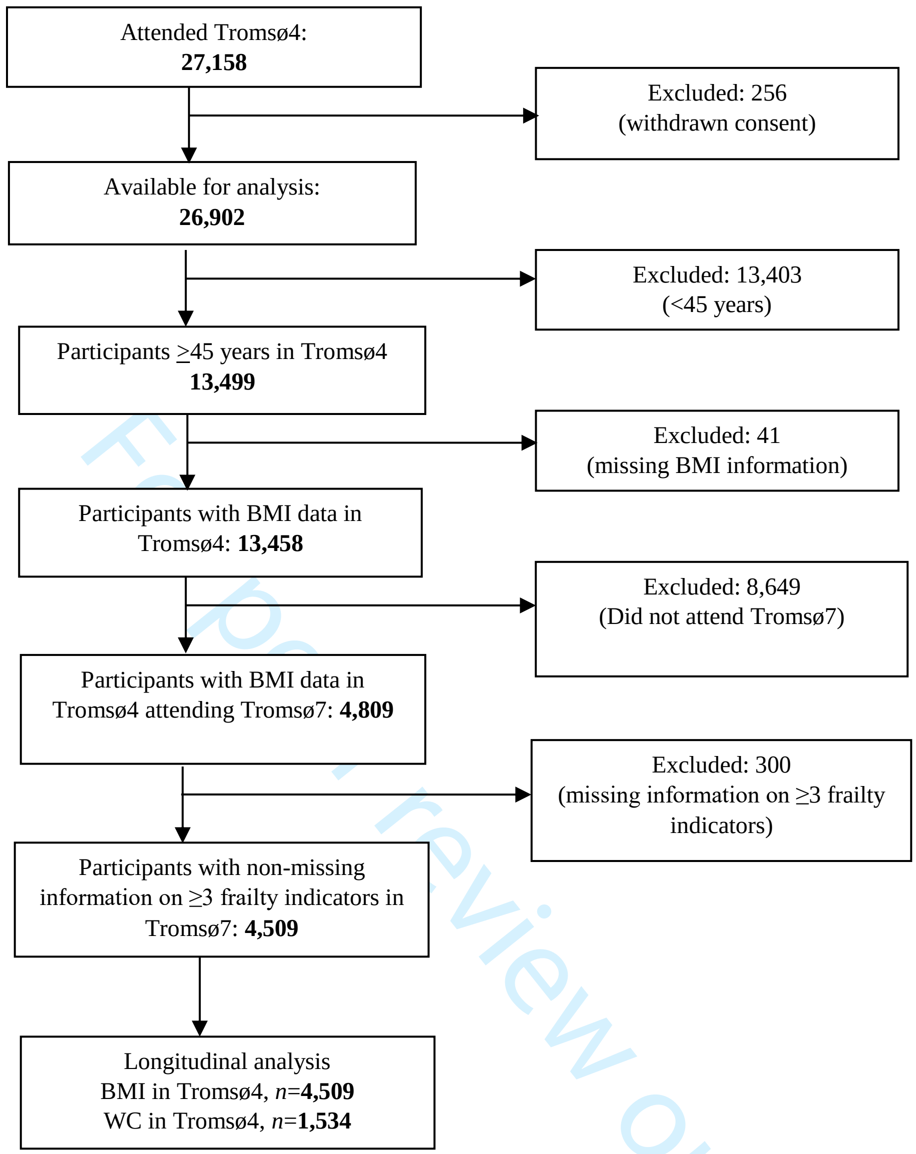


Figure 1 Flowchart displaying participants' inclusion and exclusion

SUPPLEMENTARY TABLES

Supplementary Table 1 Comparison between Fried et al.'s suggested criteria for frailty and modified frailty indicators used in this study

Frailty	Fried et al. (2001)	Current study
Exhaustion	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 day? 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 time (3–4 days) 3 = Most of the time **Exhausted: "A moderate amount of time (3–4 days)" or "Most of the time"**	Hopkins Symptom Checklist (HSCL-10): During the last week, have you experienced that everything is a struggle? 1 = No complaint 2 = Little complaint 3 = Pretty much 4 = Very much **Exhausted: "Pretty much" or "Very much"**
Physical activity	Minnesota Leisure Time Activity Questionnaire asking about walking, chores (moderately strenuous), mowing the lawn, raking, gardening, hiking, jogging, biking, exercise, cycling, dancing, aerobics, bowling, golf, singles, tennis, racquetball, calisthenics, swimming. The kcal/week expended was calculated using a standardized algorithm. Lowest 20% were identified, resulting in following cut-off for frailty: Men: <383 kcal of physical activity/week Women: <270 kcal of physical activity/week	Describe your exercise and physical exertion in leisure time over the last year (Saltin & Grimby's Scale). 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 shoveling, etc. at least 4 hours a week 4 = Participation in hard training or sports competitions, regularly several times a week **Low physical activity level: "Reading, watching TV/screen or other sedentary activity"**
Weight loss	In the last year, have you lost more than 10 pounds (4.5 kg) unintentionally (not due to dieting or exercise)? **Frail: "Yes"**	Have you involuntarily lost weight during the last 6 months? (Malnutrition Universal Screening Tool) 0 = No 1 = Yes **Lost weight: "Yes"**
Grip strength	Measured by Jamar dynamometer (kg) Maximal strength in dominant hand (3 trials) Stratified by sex and BMI quartiles. Lowest 20% were identified, resulting in the following cut-off for frailty: **Men** — **Cut-off for grip strength (kg) criterion for frailty** BMI ≤24 — ≤29 kg BMI 24.1–26 — ≤30 kg BMI 26.1–28 — ≤30 kg BMI >28 — ≤32 kg **Women** BMI ≤23 — ≤17 kg BMI 23.1–26 — ≤7.3 kg BMI 26.1–29 — ≤18 kg BMI >29 — ≤21 kg	Measured by Jamar dynamometer (kg) Strongest measurement from 3 trials in each hand Stratified by sex and BMI quartiles as per Fried's definition: **Men** — **Cut-off for grip strength (kg) criterion for frailty** BMI ≤24 — ≤29 kg BMI 24.1–26 — ≤30 kg BMI 26.1–28 — ≤30 kg BMI >28 — ≤32 kg **Women** BMI ≤23 — ≤17 kg BMI 23.1–26 — ≤17.3 kg BMI 26.1–29 — ≤18 kg BMI >29 — ≤21 kg

Frailty	Fried et al. (2001)	Current study
Walking speed	Time to walk (seconds) 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 frailty: **Men** **Cut-off for walking speed criterion for frailty** Height ≤173 cm ≥7 s Height >173 cm ≥6 s **Women** Height ≤159 cm ≥7 s Height >159 cm ≥6 s	SPPB: Short Physical Performance Battery – walking test Fastest of two times (seconds) to walk 4 m stratified by sex and height according to Fried's gender-specific cut-off. Converted to feet from meters. **Men** **Cut-off for walking speed criterion for frailty** Height ≤173 cm ≥7 s Height >173 cm ≥6 s **Women** Height ≤159 cm ≥7 s Height >159 cm ≥6 s
Frailty status	Frailty score: 0 = Robust 1–2 = Pre-frail ≥3 = Frail	Frailty score: 0 = Robust 1–2 = Pre-frail ≥3 = Frail Pre-frailty/frailty score: 0 = Robust ≥1 = Pre-frail/frail

Supplementary Table 2 Descriptive characteristics of participants at follow-up: The Tromsø Study 2015-2016

	Frailty status		
	Robust (% (n)) 70.5 (3,179)	**Pre-frail/ frail (% (n)) 29.5 (1,330)**	***P* value**
Age in years, mean (SD)	72.1 (5.1)	73.8 (5.9)	<0.001[a]
Women	50.6 (1608)	55.0 (732)	0.006
Smoking status			
Current smokers	8.3 (262)	14.4 (188)	
Former smokers	53.2 (1,674)	50.8 (666)	<0.001
Never	38.4 (1,208)	34.8 (456)	
Married or cohabiting	71.0 (2,258)	64.6 (859)	<0.001
Self-perceived health – good	69.4 (2,178)	43.2 (566)	<0.001
Social support – enough good friends	87.4 (2,676)	82.0 (1,047)	<0.001
Educational level			
Primary/Partly secondary	39.1 (1,201)	50 (632)	
Upper secondary	26.6 (817)	26.2 (331)	<0.001
College/University short	16.3 (500)	12.2 (154)	
College/University long	18.1 (556)	11.6 (147)	
Alcohol intake			
Never/Abstaining	11.2 (352)	17.4 (229)	
Infrequent drinkers	58.6 (1,846)	61.0 (803)	<0.001
Frequent drinkers	30.3 (954)	21.6 (284)	
Prevalent diseases			
Pulmonary disease[b]	14.6 (444)	19.9 (250)	<0.001
Coronary heart disease[c]	13.7 (415)	19.3 (241)	<0.001
Diabetes	7.3 (224)	14.8 (186)	<0.001
Cancer	15.6 (475)	19.3 (243)	0.003
Stroke	5.1 (154)	8.1 (101)	<0.001
Peptic ulcer	–	–	<0.001
Comorbidity	89.8 (2,800)	82.4 (1,075)	<0.001
BMI categories			
Underweight	0.5 (17)	1.4 (18)	
Normal	30.0 (951)	24.5 (323)	<0.001
Overweight	49.4 (1,566)	41.4 (547)	
Obese	20.1 (639)	32.7 (432)	
WC categories			
Normal	22.6 (716)	17.1 (225)	
Moderately high	28.0 (888)	21.3 (281)	<0.001
High	49.4 (1,569)	61.6 (812)	

Values are percentage (number); P value: χ^2 test for categorical variables P value: [a]Student's t-test; [b]including asthma/chronic bronchitis/emphysema; [c]including angina pectoris/myocardial infarction. BMI, body mass index; WC, waist circumference.

BMI categories
Underweight: <18.5 kg/m^2
Normal: 18.5–24.9 kg/m^2
Overweight: 25.0–29.9 kg/m^2
Obesity: ≥30 kg/m^2

WC categories
Normal: men ≤94 cm; women ≤80 cm
Moderately high: men 95–102 cm; women 81–88 cm
High: men >102 cm; women >88 cm

Supplementary Table 3 Descriptive baseline characteristics of Tromsø4 participants who attended Tromsø7 versus those who did not: The Tromsø Study 1994–2016

	Frailty status		
	Not attended Tromsø7 n = 8,649 (% (n))	**Attended Tromsø7 n = 4,809 (% (n))**	***P* value**
Age in years, mean (SD)	63.2 (11.0)	52.0 (5.8)	<0.001[a]
Women	52.4 (4,533)	52.4 (2520)	0.990
Smoking status			
Current smokers	33.7 (2,916)	29.4 (1,414)	
Former smokers	33.4 (2,886)	35.6 (1,714)	<0.001
Never	32.9 (2,847)	(34.9) 1,681	
Married or cohabiting	64.7 (5,568)	(82.7) 3,977	<0.001
Self-perceived health status – good	50.7 (4,378)	(70.3) 3,379	<0.001
Social support – enough good friends	83.0 (5,775)	(82.2) 3,590	0.330
Educational level			
Primary/Partly secondary	57.2 (4,911)	(36.9) 1,768	
Upper secondary	27.5 (2,362)	(34.1) 1,633	<0.001
College/University short	8.1 (696)	(14.9) 716	
College/University long	7.2 (622)	(14.1) 678	
Alcohol intake			
Never/Abstaining	24.5 (2,108)	(10.2) 491	
Infrequent drinkers	66.8 (5,749)	(76.2) 3655	<0.001
Frequent drinkers	8.7 (744)	(13.5) 649	
Prevalent diseases			
Pulmonary disease[b]	16.2 (1,097)	(9.9) 430	<0.001
Coronary heart disease[c]	14.8 (1,281)	(3.1) 149	<0.001
Diabetes	4.3 (374)	(0.5) 25	<0.001
Cancer	7.7 (517)	(3.1) 132	<0.001
Stroke	3.7 (318)	(0.7) 33	<0.001
Ulcer	14.1 (908)	(7.8) 333	<0.001
Comorbidity	9.9 (858)	(2.3) 36	<0.001
BMI categories			
Underweight	1.7 (149)	0.5 (22)	
Normal	40.0 (3,463)	44.9 (2,169)	<0.001
Overweight	42.3 (3,659)	43.5 (2,094)	
Obesity	15.9 (1,378)	11.1 (533)	
WC categories			
Normal	39.0 (1,784)	45 (765)	
Moderately high	29.7 (1,356)	32.6 (554)	<0.001
High	31.3 (1,434)	22.4 (381)	

Values are percentage (number); P value: χ^2 test for categorical variables P value: [a]Student's t-test; [b]including asthma/chronic bronchitis/emphysema; [c]including angina pectoris/myocardial infarction. BMI, body mass index; WC, waist circumference.

BMI categories
Underweight: <18.5 kg/m^2
Normal: 18.5–24.9 kg/m^2
Overweight: 25.0–29.9 kg/m^2
Obesity: ≥30 kg/m^2

WC categories
Normal: men ≤94 cm; women ≤80 cm
Moderately high: men 95–102 cm; women 81–88 cm
High: men >102 cm; women >88 cm

Supplementary Table 4 Cross-sectional association between BMI and WC, and pre-frailty/frailty: The Tromsø Study 2015–2016

	Frailty status		Model 1	Model 2
	Robust (% (*n*))	**Pre-frail/frail (% (*n*))**	**OR (95% CI)**	**OR (95% CI)**
	70.5 (3179)	29.5 (1330)		
BMI, kg/m^2				
Underweight	0.5 (17)	1.4 (18)	2.93 (1.48–5.83)	2.32 (1.09–4.94)
Normal	30.0 (951)	24.5 (323)	Ref.	Ref.
Overweight	49.4 (1,566)	41.4 (547)	1.07 (0.91–1.26)	1.03 (0.86–1.23)
Obesity	20.1 (639)	32.7 (432)	2.14 (1.79–2.56)	1.88 (1.54–2.30)
WC, cm				
Normal	22.6 (716)	17.1 (225)	Ref.	Ref.
Moderately high	28.0 (888)	21.3 (281)	1.02 (0.83–1.25)*	1.01 (0.81–1.26)*
High	49.4 (1,569)	61.6 (812)	1.69 (1.42–2.01)*	1.45 (1.20–1.76)*

Model 1: minimally adjusted for age and sex (*excluding sex) at Tromsø7.
Model 2: adjusted for age, sex, educational level, smoking status, alcohol intake, comorbidities, social support, and self-perceived health (*excluding sex) at Tromsø7.
BMI, body mass index; CI, confidence interval; OR: odds ratio; WC, waist circumference.

Supplementary Table 5 Longitudinal association between BMI and WC, combined profiles and trajectories, and pre-frailty/frailty: The Tromsø Study 1994–2016

	Frailty status		Model 1	Model 2
	Robust (%) (n)	Pre-frail/frail (≥2) (%) (n)	OR (95% CI)	OR (95% CI)
BMI, kg/m²	n= 2925	n= 1125		
Underweight	0.4 (10)	0.7 (8)	2.28 (0.89–5.88)	1.37 (0.49–3.89)
Normal	48.0 (1404)	40.1 (451)	Ref.	Ref.
Overweight	43.0 (1259)	41.7 (469)	1.16 (0.99–1.36)	1.16 (0.99–1.36)
Obesity	8.6 (252)	17.5 (197)	2.38 (1.92–2.95)	2.31 (1.83–2.92)
WC, cm	n= 714	n = 387		
Normal	51.5 (368)	39.0 (151)	Ref.	Ref.
Moderately high	31.1 (222)	33.1 (128)	1.40 (1.05–1.87)*	1.50 (1.10–2.05)*
High	17.4 (124)	27.9 (108)	2.10 (1.52–2.89)*	2.19 (1.54–3.14)*
BMI and WC profile, baseline	n= 650	n = 347		
Normal BMI and normal WC	36.6 (238)	30.8 (107)	Ref.	Ref.
Normal BMI and moderately high/high WC	8.0 (52)	6.4 (22)	0.94 (0.54–1.63)*	0.92 (0.50–1.66)
Overweight and normal WC	15.4 (100)	9.2 (32)	0.73 (0.46– 1.15)*	0.74 (0.45– 1.20)
Overweight and moderately high/high WC	32.0 (208)	34.9 (121)	1.31 (0.95– 1.81)*	1.47 (1.04–2.08)
Obesity and moderately high/high WC	8.0 (52)	18.7 (65)	2.73 (1.77– 4.20)*	2.91 (1.83–4.65)
BMI trajectories	n= 653	n = 348		
Stable normal BMI	26.9 (176)	22.1 (77)	Ref.	Ref.
Stable overweight	46.6 (304)	41.1 (143)	1.16 (0.83–1.63)	1.14 (0.79–1.63)
Overweight to obese	22.4 (146)	25.9 (90)	1.53 (1.04–2.24)	1.55 (1.02–2.35)
Increasing obesity	4.1 (27)	10.9 (38)	3.35 (1.90–5.90)	3.17 (1.72–5.85)
WC trajectories (women)	n= 287	n = 172		
Normal to moderately high WC	25.5 (73)	20.4 (35)	Ref.	Ref.
Moderately high to high WC	50.5 (145)	38.9 (67)	0.98 (0.60–1.62)*	1.12 (0.65–1.93)*
Gradually increasing high WC	20.9 (60)	33.7 (58)	1.99 (1.15–3.43)*	2.02 (1.10–3.71)
Steeply increasing high WC	3.1 (9)	7.0 (12)	2.63 (1.01–6.86)*	3.30 (1.09–10.04)*
WC trajectories (men)	n= 366	n = 176		
Normal WC	21.6 (79)	17.6 (31)	Ref.	Ref.
Stable moderately high WC	41.5 (152)	36.4 (64)	1.09 (0.66–1.81)*	1.03 (0.60–1.76)*
Moderately high to high WC	32.2 (118)	29.6 (52)	1.17 (0.69–1.99)*	1.06 (0.60–1.87)*
Increasing high WC	4.6 (17)	16.5 (29)	4.51 (2.17–9.38)*	4.36 (1.94–9.80)*

[#]Analysis was restricted to individuals who were <60 years at Tromsø4
Model 1: adjusted for age and sex (*excluding sex) at baseline.
Model 2: adjusted for age, sex, educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level (*excluding sex) at baseline.
BMI, body mass index; CI, confidence interval; OR, odds ratio; WC, waist circumference.

Supplementary Table 6 Longitudinal association between BMI and WC, combined profiles and trajectories, and pre-frailty/frailty (frailty score ≥ 2): The Tromsø Study 1994–2016

	Frailty status		Model 1	Model 2
	Robust (%) (n)	Pre-frail/frail (≥2) (%) (n)	OR (95% CI)	OR (95% CI)
BMI, kg/m²	n= 2925	n= 199		
Underweight	0.4 (10)	0.5 (1)	1.45 (0.18–11.98)	0.95 (0.11–7.85)
Normal	48.0 (1404)	37.7 (75)	Ref.	Ref.
Overweight	43.0 (1259)	38.7 (77)	1.22 (0.87–1.71)	1.18 (0.82–1.71)
Obesity	8.6 (252)	23.1 (46)	3.47 (2.33–5.18)	3.27 (2.09–5.08)
WC, cm	n= 714	n = 88		
Normal	51.5 (368)	30.7 (27)	Ref.	Ref.
Moderately high	31.1 (222)	36.4 (32)	1.97 (1.15–3.38)*	1.98 (1.10–3.54)*
High	17.4 (124)	32.9 (29)	3.20 (1.82–5.64)*	3.18 (1.71–5.93)*
BMI and WC profile, baseline	n= 650	n = 81		
Normal BMI and normal WC	36.6 (238)	27.2 (22)	Ref.	Ref.
Normal BMI and moderately high/high WC	8.0 (52)	8.6 (7)	1.45 (0.59–3.59)	1.41 (0.52–3.86)
Overweight and normal WC	15.4 (100)	3.7 (3)	0.33 (0.09– 1.13)	0.37 (0.11– 1.31)
Overweight and moderately high/high WC	32.0 (208)	38.3 (31)	1.65 (0.92–2.95)	1.81 (0.97–3.38)
Obesity and moderately high/high WC	8.0 (52)	22.2 (18)	3.79 (1.89– 7.62)	3.66 (1.71–7.81)

#Analysis was restricted to individuals who were <60 years at Tromsø4 and had frailty score ≥2
Model 1: adjusted for age and sex (*excluding sex) at baseline.
Model 2: adjusted for age, sex, educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level (*excluding sex) at baseline.
BMI, body mass index; CI, confidence interval; OR, odds ratio; WC, waist circumference.

Supplementary Table 7 Longitudinal association between BMI and WC, and pre-frailty/frailty among individuals with information on all five frailty criteria: The Tromsø Study 1994–2016

	Frailty status		Model 1	Model 2
	Robust (%) (n)	Pre-frail/frail (%) (n)	OR (95% CI)	OR (95% CI)
	70.4% (2016)	29.6% (848)		
BMI, kg/m²				
Underweight	0.4 (8)	0.7 (6)	1.98 (0.67–5.84)	0.97 (0.28–3.23)
Normal	48.4 (976)	40.1 (340)	Ref.	Ref.
Overweight	42.8 (862)	42.9 (364)	1.19 (0.99–1.42)	1.18 (0.97–1.43)
Obesity	8.4 (170)	16.3 (168)	2.36 (1.82–3.05)	2.28 (1.72–3.01)
WC, cm	n = 600	n = 350		
Normal	53.3 (320)	40.9 (143)	Ref.	Ref.
Moderately high	31.3 (188)	34.0 (119)	1.40 (1.03–1.90)*	1.50 (1.08–2.08)*
High	15.3 (92)	25.1 (88)	2.15 (1.51–3.08)*	2.15 (1.46–3.18)*

Model 1: adjusted for age and sex (*excluding sex) at baseline.
Model 2: adjusted for age, sex, educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level (*excluding sex) at baseline.
BMI, body mass index; CI, confidence interval; OR, odds ratio; WC, waist circumference.

Supplementary Table 8 Longitudinal association between BMI and WC, and frailty components: The Tromsø Study 1994–2016

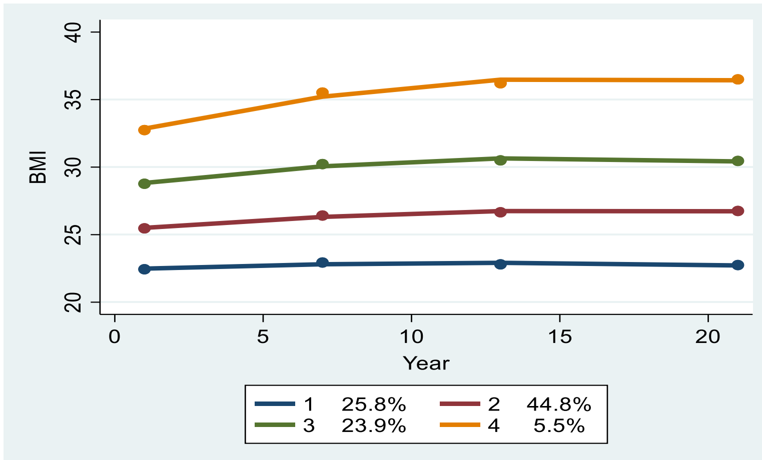
	Model 1 OR (95% CI)	Model 2 OR (95% CI)
Low grip strength		
BMI, kg/m²		
Underweight	0.85 (0.11–6.63)	0.78 (0.10–6.17)
Normal	Ref.	Ref.
Overweight	1.45 (1.05–2.00)	1.34 (0.95–1.89)
Obesity	2.00 (1.31–3.05)	1.52 (0.95–2.43)
WC, cm		
Normal	Ref.	Ref.
Moderately high	0.99 (0.58–1.68)*	0.92 (0.51–1.65)*
High	1.40 (0.81–2.43)*	1.37 (0.75–2.50)*
Low walking speed		
BMI, kg/m²		
Underweight	4.51 (1.20–16.95)	3.03 (0.64–14.35)
Normal	Ref.	Ref.
Overweight	1.63 (1.12–2.37)	1.67 (1.12–2.48)
Obesity	3.32 (2.13–5.16)	3.15 (1.96–5.07)
WC, cm		
Normal	Ref.	Ref.
Moderately high	2.24 (1.27–3.94)*	2.52 (1.38–4.63)*
High	2.65 (1.45–4.85)*	2.35 (1.19–5.63)*
Exhaustion		
BMI, kg/m²		
Underweight	1.72 (0.22–13.18)	1.62 (0.20–13.24)
Normal	Ref.	Ref.
Overweight	1.11 (0.74–1.65)	1.06 (0.69–1.64)
Obesity	1.39 (0.793–2.42)	1.25 (0.69–2.27)
WC, cm		
Normal	Ref.	Ref.
Moderately high	1.67 (0.75–3.72)*	1.67 (0.72–3.89)*
High	1.74 (0.72–4.20)*	1.69 (0.66–4.29)*
Unintentional weight loss		
BMI, kg/m²		
Underweight	2.84 (0.92–8.79)	2.15 (0.60–7.76)
Normal	Ref.	Ref.
Overweight	0.63 (0.49–0.82)	0.64 (0.49–0.85)
Obesity	0.68 (0.45–1.03)	0.70 (0.46–1.08)
WC, cm		
Normal	Ref.	Ref.
Moderately high	0.99 (0.64–1.55)*	1.10 (0.70–1.73)*
High	0.57 (0.57–1.03)*	0.56 (0.30–1.07)*
Low physical activity		
BMI, kg/m²		
Underweight	–	–
Normal	Ref.	Ref.
Overweight	1.42 (1.16–1.74)	1.43 (1.15–1.79)
Obesity	3.62 (2.81–4.68)	3.71 (2.80–4.90)
WC, cm		
Normal	Ref.	Ref.
Moderately high	1.85 (1.24–2.78)*	1.71 (1.10–2.66)*
High	4.47 (2.97–6.72)*	4.94 (3.15–7.76)*

[#] Analysis was restricted to individuals who were <60 years at Tromsø4
Model 1: adjusted for age and sex (*excluding sex) at baseline.
Model 2: adjusted for age, sex, educational level, marital/cohabitation status, smoking status, alcohol intake, social support, self-perceived health, and physical activity level (*excluding sex) at baseline.
BMI, body mass index; CI, confidence interval; OR, odds ratio; WC, waist circumference.

SUPPLEMENTARY FIGURES

Supplementary Figure 1 Trajectories of individuals with repeated body mass index measurements between Tromsø4 and Tromsø7: The Tromsø Study 1994–2016.

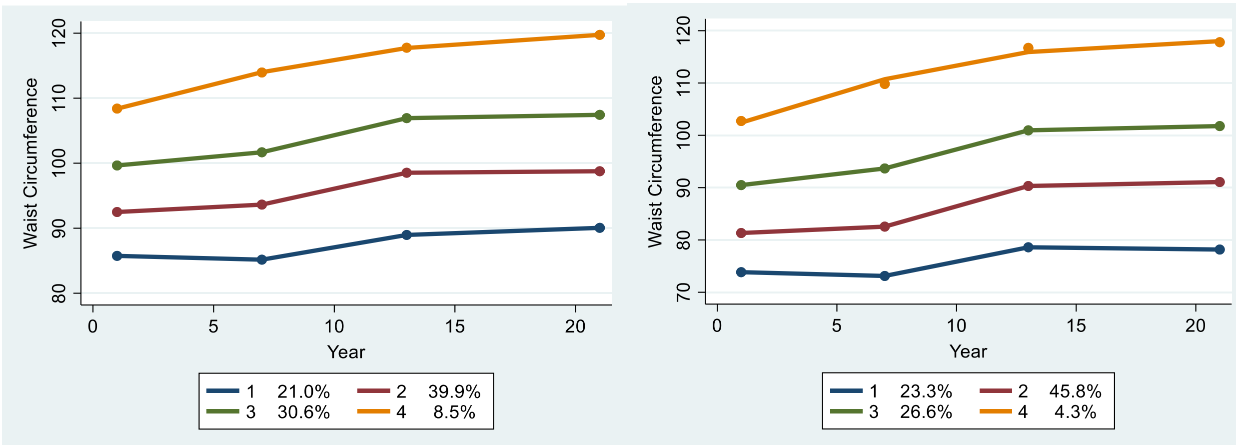
(n = 1,391)



Group 1	Stable normal weight	25.8%
Group2	Stable overweight	44.8%
Group 3	Overweight to obesity	23.9%
Group 4	Increasing obesity	5.5%

Supplementary Figure 2 Trajectories of individuals with repeated waist circumference measurements between Tromsø4 and Tromsø7: The Tromsø Study 1994–2016.

(Males: n = 731; females n = 660)



	Male	
Group 1	Stable normal WC	21.00%
Group 2	Stable moderately high WC	39.90%
Group 3	Moderately high to high WC	30.60%
Group 4	Increasing high WC	8.5 %

	Female	
Group 1	Stable normal WC	23.30%
Group 2	Moderately high to high WC	45.80%
Group 3	Gradually increasing high WC	26.60%
Group 4	Steeply increasing high WC	4.30%

Research checklist

	Item No	Content covered	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	√ (1-2)
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	√ (3)
Objectives	3	State specific objectives, including any pre-specified hypotheses	√ (3)
Methods			
Study design	4	Present key elements of study design early in the paper	√ (4)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	√ (4)
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed (*b*) Flow chart explaining inclusion and exclusion of partcipants	√ (4)
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	√ (4,5,6)
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	√ (4,5)
Bias	9	Describe any efforts to address potential sources of bias	√ (6)
Study size	10	Explain how the study size was arrived at	√ (4)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	√ (4,5,6)
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	√ (6)
Results			
Participants	13	(a) Information on participants	√ (4)
Descriptive data	14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	√ (7, 8)
Outcome data	15	Report numbers of outcome events or summary measures over time	√ (8-11)

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	√ (9-11)
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	√ (9-11)
Discussion			
Key results	18	Summarise key results with reference to study objectives	√ (11)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	√ (13)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	√ (11-14)
Generalisability	21	Discuss the generalisability (external validity) of the study results	√ (13-14)
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	√ (15)