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Type 2 diabetes as a predictor of muscle strength decline over 11 years among men and women aged 55 and older

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Abstract

Background: Long-term associations between type 2 diabetes, pre-diabetes and muscle strength are obscure in older adults. The aim of this study was to examine type 2 diabetes as a predictor of handgrip strength decline during an 11-years follow-up among men and women aged 55 years.

Methods: We used Finnish population-based Health 2000 Survey and its follow-up measurements in 2011. The study population consisted of 1190 individuals, aged 55-86 years at baseline. Baseline fasting glucose level or use of diabetes medication were used to categorize the participants into diabetes (≥7.0 mmol/l), pre-diabetes (≥6.1 mmol/l but < 7.0 mmol/l) and non-diabetes (<6.1 mmol/l) groups. Handgrip strength was measured at baseline and during 11-year follow-up.

Results: Mean handgrip strength at baseline did not differ between diabetes groups in men or women. Among men during the 11-year follow-up, decline in muscle strength was significantly greater among diabetes group (-121.1 Newton [N], 95% CI -164.7 to -77.5) compared to non-diabetes group (-88.9 N, 95% CI -125.7 to -52.1) after adjusting for age, education, lifestyle factors and chronic conditions. Among women, muscle strength decline did not differ between diabetes, pre-diabetes or non-diabetes group after adjusting for all potential covariates, the results being -48.1 N (95% CI -73.8 to -22.3), -35.5 N (95% CI -62.9 to -8.1) and -39.4 N (95% CI -64.4 to -14.3), respectively.

Conclusions: The presence of type 2 diabetes was associated with greater muscle strength decline among older men but not among older women.

Introduction

Type 2 diabetes is a common metabolic disease which prevalence increases with age. It has been estimated that the proportional increase in the number of people with diabetes will be the largest among persons aged 60-79 in the upcoming years [1]. Diabetes is a growing public health concern, but it also affects negatively older people's functioning and quality of life.

Type 2 diabetes is associated with muscle dysfunction [2], both functional [3-5] and cognitive [4] impairments, and increased risk of other chronic conditions, such as cardiovascular diseases [6, 7], sarcopenia [8] and frailty [9]. The pathogenesis, which can lead to functional limitation and disability among diabetics, is complex and still poorly understood. Diabetes is preceded by glucose metabolism dysregulation and insulin resistance, and individuals with pre-diabetes status [10] with impaired fasting glucose (usually defined as ≥6.1 mmol/L but <7.0 mmol/L) are at higher risk to progress to type 2 diabetes. Both pre-diabetes and diabetes are more common in older than in younger individuals [2].

Skeletal muscle is the major site of glucose uptake and it has a critical role in maintaining blood glucose homeostasis. In turn glucose is necessary for muscle contraction. Insulin increases glucose uptake and helps to regulate protein metabolism in the muscle [11, 12]. Insulin can also repress the whole-body proteolysis and in that way induce an anabolic state [11, 13, 14] . Insulin resistance could be a predictor of poor muscle health, irrespective of diabetes status. With aging, the secretion of insulin decreases [15] . The ability of insulin to stimulate skeletal muscle glucose transport is impaired in individuals with type 2 diabetes [11] and the effects of insulin in tissue are weaker than normally. In addition to glucose metabolism dysregulation and insulin resistance, also muscle fat infiltration[2] and low-grade chronic inflammation [16, 17] have been shown to be associated with the muscle strength decline among people with type 2 diabetes.

Earlier cross-sectional studies [18, 19, 20] have found a strong relationship between type 2 diabetes and lower muscle strength among people aged 65 and older. Thus, in addition to the fundamental biological mechanisms of diabetes to the muscle, it is possible that diabetes can also accelerate the age-related loss of muscle mass and muscle strength. However, very little research has been conducted on the role of type 2 diabetes on muscle strength decline. Park et al. [17] showed that during a three-year follow-up, 70 to 79-year old people with diabetes lost almost 14% of knee extensor strength while the loss among those without diabetes was 9%. However, the changes in hand grip strength during the follow-up did not differ between those with and without diabetes [17].

Since the deteriorating effect of type 2 diabetes on muscle strength may aggravate over time, it would be important to examine long-term effects of type 2 diabetes on muscle strength decline. To the best of our knowledge, however, there are no previous studies analyzing how type 2 diabetes, and pre-diabetes, affect muscle strength over a longer time period.

By utilizing longitudinal data from the Finnish Health 2000 Survey, a representative population-based cohort, we investigated the associations between type 2 diabetes and pre-diabetes and handgrip strength decline over an 11-year follow-up among men and women aged 55 years and older at baseline. Our hypothesis was that older adults with type 2 diabetes and pre-diabetes would have a greater decline in muscle strength than people with normal glucose metabolism.

Material and methods

Study population

This study is based on the Health 2000 Survey, which is a comprehensive nationwide health interview and examination survey carried out in Finland in 2000–2001 and its follow-up measurements 11 years later in 2011–2012. All persons who had been included in the Health 2000 Survey sample and had not refused further contacts were re-invited 11 years later. Details of the design and implementation of the Health 2000 Survey and its follow-up have been reported elsewhere [21, 22]. The original Health 2000 Survey was based on two-stage stratified cluster sample comprising 8,028 adults aged 30 years or older (of which 3392 were 55 years and older), living in mainland Finland either in the community or in an institution. Of them 5903 participated in the follow-up 11 years later (73% participation rate) [22]. For the present study, the target population were participants who were 55 years or older, had information on type 2 diabetes and handgrip strength measured at baseline (n=2792). Of them 1200 also had handgrip strength measured in 2011. After excluding 10 outliers i.e. participants whose standardized change of muscle strength (z-score) was under -3.29 or over 3.29, the analyses covered 1190 participants.

All participants signed a written informed consent form approved by the Ethical Committee for Epidemiology and Public Health in the Hospital District of Helsinki and Uusimaa in Finland.

Assessment of diabetes status

Diabetes status (diabetic, pre-diabetic, non-diabetic) was defined at the baseline and after 11-year follow-up based on the level of fasting glucose or the information about the diabetes medication. Fasting blood samples were drawn during the clinical examination. The samples were centrifuged at the examination site, stored in deep freezers at -20°C, and transferred within

1 week to the National Public Health Institute to be stored in deep freezers at -70°C until used for laboratory analysis. Level of fasting glucose was determined using the glucose dehydrogenase method (Diagnostica, Merck, Darmstadt, Germany) and radioimmunoanalysis (Pharmacia, Uppsala, Sweden), respectively. The interassay coefficient of variation for glucose was 2.0%. The participant was considered to have diabetes, if fasting glucose was 7.0 mmol/l or more. Pre-diabetes, impaired fasting glucose, was defined as fasting glucose ≥6.1 mmol/l but <7.0 mmol/l and non-diabetes as fasting glucose <6.1 mmol/l [10]. If there was no data on the participant's fasting glucose (n=6), information about diabetes medications from the health questionnaire was used. The participant was considered to have diabetes if she/he reported taking any medication for diabetes.

Measurement of muscle strength

Maximal handgrip strength was measured using a dynamometer on the dominant hand in a sitting position. The dominant hand was defined as the writing hand. Measurement was repeated twice and if the results differed more than 10%, a third attempt was conducted. The best result was chosen for the analysis. At the baseline, the measurement was conducted with an adjustable dynamometer (Good Strength, IGS01, Metitur Oy, Jyväskylä, Finland) and results were recorded in kilograms (kg). At the follow-up, handgrip strength was measured using a hand-held Jamar/Saehan dynamometer (Sammong Preston Rolyan 2003) because Metitur's dynamometer was no longer available. In Jamar/Saehan dynamometer the result was recorded in Newtons (N) [23]. In order to calculate the muscle strength change between the follow-up and baseline measures and compare the strength results, kilograms were converted to Newtons by multiplying with 9.81.

To assess the comparability of the two handgrip strength measurement devices, 40 volunteers were measured with both dynamometers. The statistical comparison was conducted using Ordinary Least Products (OLP) regression method [24]. The Intraclass Correlation Coefficient (ICC) estimates varied from 0.81 (only women) to 0.96 (men and women), indicating fair to excellent agreement[23]. Based on these results, it was feasible to calculate the absolute handgrip strength change between the baseline and follow-up measurements.

Covariates

Based on the association with type 2 diabetes and hand grip strength, the following covariates were included: education, body mass index (BMI), hormone replacement therapy (HRT), physical activity, alcohol consumption, smoking, and chronic conditions. Except for BMI, information on all these variables was collected with questionnaire at the baseline. Information of BMI, physical activity and chronic conditions at follow-up were also utilized in the analysis.

The level of education was classified as basic education (0-9 years), intermediate education (10-12 years) and higher education (13 years or more). To calculate *BMI*, body weight was measured a part of body composition assessment (InBody 3.0, Biospace, Soul, South Korea) in kilograms (kg) and height was measured without socks, using a wall-mounted stadiometer (cm). If measured data were missing, self-reported information about weight and height were used. BMI was calculated as weight in kilograms divided by the square of height in meters (kg/m^2). Based on the self-reported information about use of *HRT* at baseline, female participants were classified as HRT users, former users and non-users. *Physical activity* was classified as sedentary, moderately active or regular/very active based on a physical activity questionnaire in which participants assessed their average level of physical activity. *Alcohol consumption* was assessed as average weekly consumption (grams/week) during the preceding month and

classified as no alcohol use, moderate use and heavy use. The limit for heavy alcohol use was set at 280 g/week for men and 140 g/week for women [25]. *Smoking status* was classified into never smokers, former smokers and current smokers. *Chronic conditions* used in the present study were hypertension, coronary heart disease (angina pectoris or myocardial infarction), heart failure, osteoarthritis (knee or hip), inflammatory arthritis, pulmonary diseases (asthma, chronic obstructive pulmonary disease, and chronic bronchitis), stroke, Parkinson's disease, chronic mental disorders and cancer.

Statistical analysis

Characteristics of the participants are presented as percentages or means with standard errors of the means (SEM) by diabetes status and separately for men and women. Differences in characteristics between the groups were determined using one-way analysis of variance (ANOVA) for continuous variables and chi-squared test (χ^2) for categorical variables. Average level of muscle strength by sex and diabetes status was examined with ANOVA.

Muscle strength change was calculated as a difference between muscle strength in 2011 and in 2000. This variable was used as an outcome in linear regression analyses where diabetes status was a predictor. Unstandardized regression coefficients with their 95% confidence intervals (CI) were estimated for four different models. In Model 1, the independent variables were diabetes status and baseline muscle strength. In Model 2, age and education were added. In Model 3, baseline BMI, HRT, physical activity, alcohol consumption and smoking status were added and in Model 4 also baseline chronic conditions were included. In Model 5 also follow-up diabetes status was added. Linear regression models were performed separately for men and women because the effect of diabetes was different for women than men (sex * diabetes

interaction, p= 0.007). Because of multiple comparisons for the group variable, the Bonferroni adjustment was used for correcting the significance level.

Participants aged 80 years or older were oversampled (2:1) in relation to their proportion in the population at baseline Health 2000 Survey. The data were weighted to reduce bias due to nonresponse and to correct the oversampling in the age group of 80 years and older in order to represent the Finnish population. The complex sampling design was taken into account by using a special package for complex samples in SPSS, version 22.0 (SPSS Inc., Chicago, IL), and by using survey procedures (*svy* prefix command) in Stata 14.0 (College Station, Texas).

Results

Table 1 shows characteristics of the participants by sex and baseline diabetes status. At baseline, 8% of men and 6% of women had diabetes and 16% and 11% had pre-diabetes, respectively. The mean age for men was slightly lower (62.9 years; 95% CI 62.4-63.4) than in women (63.8 years; 95% CI 63.3-64.3), but age did not differ across diabetes groups in men or women. Men and women with diabetes were more often obese (BMI ≥30 kg/m^2) than pre-diabetes and non-diabetes individuals (men: diabetes 47%, pre-diabetes 33%, non-diabetes 20%, women: diabetes 61%, pre-diabetes 34%, non-diabetes 29%). Men and women with diabetes had more hypertension and heart failure as compared to men and women without diabetes. In addition, osteoarthritis was more common among men with diabetes than men with pre-diabetes or non-diabetes. Among women, current use of HRT differed statistically significantly between groups being 37%, 32% and 20% in women with diabetes, pre-diabetes and non-diabetes, respectively.

At baseline, mean handgrip strength did not differ between men with diabetes, pre-diabetes and non-diabetes (445.7 N, 95% CI 426.4- 465.1; 446.6 N, 95% CI 427.3-466.0; 448.5 N, 95% CI 438.7-458.4, Fig. 1, Supplementary Fig 1). During the 11-year follow-up, decline in muscle strength was statistically significantly greater among men with diabetes (-97.4 N, 95% CI -116.6 to -78.2) as compared with non-diabetes men (-64.7 N, 95% CI -73.6 to -55.8) (Table 2, Model 2). Percentual decline in muscle strength for men with diabetes, pre-diabetes and non-diabetes was 22%, 18% and 14%, respectively. The statistically significant difference in muscle strength decline between diabetic and non-diabetic men persisted after further adjustments for lifestyle factors (Model 3) and chronic conditions (Model 4). The muscle strength decline in the pre-diabetes group did not differ statistically significantly from diabetes or non-diabetes groups in men in any model.

Also, in women, the mean handgrip strength at baseline did not differ between diabetes pre-diabetes and non-diabetes groups (244.3 N, 95% CI 212.7-266.0; 255.3 N, 95% CI 240.7-270.0; 254.2 N, 95% CI 248.6- 259.9, Fig. 1, Supplementary Fig. 1). Muscle strength decline during 11 years did not differ between diabetes, pre-diabetes or non-diabetes women being -25.7 N (95% CI -38.9 to -12.4), -16. 8 N (95% CI -26.9 to -6.7) and -20.8 N (95% CI -25.2 to -16.3) respectively (Table 2, Model 2). During the 11-year follow-up, the muscle strength decline for women with diabetes, pre-diabetes and non-diabetes was 11%, 7% and 8%, respectively. After further adjustments for lifestyle factors, HRT and chronic conditions (Model 3 and Model 4), the differences between groups for women did not markedly change.

During an 11-year-follow-up the prevalence of diabetes increased both among men and women being 18% for men and 14% for women. Respectively, the prevalence of pre-diabetes decreased during the follow-up being 9% for men and 5% for women. To take into account the changes in diabetes status, we further adjusted the analysis for diabetes status at follow-up. However, it did not markedly change the differences between diabetes, pre-diabetes and non-diabetes group either in men or women (Table 2, Model 5).

To examine the role of selection in this study population, participants with follow-up measurements were compared to those who only participated in the baseline measurements. Among men, there was no difference in diabetes status at baseline (16% pre-diabetes and 8% diabetes among participants; 16% pre-diabetes and 13% diabetes among non-participants). Male participants of this study were statistically significantly younger (62.7, 95% CI 62.1-63.3 vs. 65.0, 95% CI 64.0-66.0) and had higher handgrip strength (448.0 N 95% CI 439.9-456.1 vs. 417.5 N, 95% CI 404.8-430.2) compared to those who were lost to follow-up. Among women, the baseline prevalence of diabetes (6% vs. 10%, p=0.002) and pre-diabetes (11% vs. 14%,

p=0.002) was significantly lower among participants compared to those who were lost to follow-up. Female participants of this study were also statistically significantly younger (63.5, 95% CI 63.1-64.0 vs. 67.6, 95% CI 66.9-68.3) and had higher (253.8 N, 95% CI 249.1-258.5 vs. 228.4 N, 95% CI 222.0-234.8) baseline handgrip strength than non-participant women.

Discussion

This study examined type 2 diabetes and pre-diabetes as predictors of muscle strength decline during an 11-year follow-up among Finnish men and women aged 55 years and older. We observed that type 2 diabetes predicts muscle strength decline among men aged 55 years and older but not among women.

The findings of this study add evidence on sparsely studied longitudinal relationship between diabetes and muscle strength decline. Previously Park et al. [17] have studied the association between diabetes and muscle strength decline in a 3-year follow-up in the Health, Aging and Body Composition Study, and they found that people aged 70-79 years with diabetes lost almost 14% of knee extensor strength compared with those without diabetes who lost 9% [17]. However, they did not separate the effects in men and women, so direct comparison to our study is difficult. In the current study, the average decline in handgrip strength was 17% in diabetes and 11% in non-diabetes individuals when men and women were considered together. Our study is the first one to report accelerated decline in muscle strength among men with type 2 diabetes compared to non-diabetes men. We did not find an association between diabetes status and muscle strength decline in women, which is in line with the prospective study by Lee et al [26].

In terms of the baseline differences, we did not find an association between baseline diabetes status and muscle strength in men or in women, which is partly in line with the study by Park et al [27] conducted among persons aged 70-79 years. They found that muscle strength did not significantly differ between diabetes and non-diabetes women but did differ in men. Some studies have observed a cross-sectional association between diabetes and muscle strength [19, 20, 28]. The discrepancy with our findings may result from the fact that we only included those

participants who participated in the follow-up, and they were younger, had better handgrip strength compared to those who dropped out during the study.

In the present study, we also examined the group of pre-diabetes. Pre-diabetes is commonly defined as blood glucose concentrations higher than normal, but lower than diabetes threshold. In our study, muscle strength decline in individuals with pre-diabetes did not differ statistically significantly from those with diabetes or non-diabetes. In addition, we did not observe differences in lifestyle factors between diabetes, pre-diabetes and non-diabetes individuals. However, the state of pre-diabetes is important to observe because persons with pre-diabetes status have a high risk to develop type 2 diabetes without lifestyle changes [29, 30].

There may be several plausible explanations why we did not observe differences in muscle strength decline in diabetes, pre-diabetes and non-diabetes women. First, women diagnosed with diabetes may be taking better care of themselves and women's attitude for lifestyle changes could be more positive than in men's. However, the results about the association between sex and preference of adherence to lifestyle and medical interventions are conflicting [31]. Another potential explanation may be menopause and HRT. During menopause, changes in steroid hormones, metabolic profile, body composition and fat distribution happen in women's body, which may also have also effect on muscle mass and muscle strength. Earlier studies have shown that increased estrogen levels with HRT helps to maintain better muscle composition and function [32, 33, 34]. In our study, there was a statistically significant difference in use of HRT between women with diabetes, pre-diabetes and non-diabetes at baseline so that HRT use was more common in diabetes and non-diabetes groups than those with pre-diabetes status. However, since we did not have information HRT use during the 11-year follow-up, we cannot

be sure about the role of HRT on the association between diabetes status and muscle strength decline.

Handgrip measurements is a reliable and widely used strength measurement which roughly reflects the level of whole-body muscle strength [35, 36]. However, the decrease in muscle strength with aging could differ between muscle groups and also diabetes can affect muscles in the upper and lower extremities differently. The results from the study by Andersen et al. [37] showed that type 2 diabetic patients younger than 70 years experienced weakness in the muscles of ankle and knee, whereas the strength at the muscles of elbow and wrist was preserved. Similarly, Park et al [17, 38] showed that among 70-79 year-old adults type 2 diabetes was associated with 3-year decline in knee extensor strength, but not decline in handgrip strength. In the cross-sectional study by Andersen et al. [37] older patients with type 2 diabetes had lower muscle strength at the ankle and knees but not at the elbow and wrist compared to people without diabetes. Earlier studies [39, 40] have shown that with aging muscle strength in lower extremities decreased more than muscle strength in upper extremities. However, the presence and severity of peripheral neuropathy related to diabetes could also have effect on differences in muscle strength and muscle strength decline in upper and lower extremities. Further studies are needed to examine long-term changes in lower extremity strength by diabetes status.

Strengths of this study include a long follow-up time and a nationally representative large sample of older adults. In the present study, diabetes status was defined at baseline and at follow-up based on the level of fasting glucose or the information about the diabetes medication. Used definition of diabetes status is valid and widely used [10]. However, we did not have information about the duration of type 2 diabetes, severity of the disease or the

therapeutic status, which could have an effect on muscle strength and changes in muscle strength.

The present study also has some limitations. First, loss due to follow-up resulted in relatively younger and healthier sample. Thus, it is likely that the observed rate of muscle strength decline is underestimated, especially in the diabetes group. Second, despite long follow-up time of our study, 11 years, we had only two measurement points. Many changes that may have effect also on muscle strength could be happed during such a long time e.g. changes in lifestyle factors or health status. Multiple measurement point could have been strengthening our findings. Third, clear limitation of this study was that at the follow-up 2011 only women below the age of 70 years were asked about menstruation and menopause, as well as hysterectomy and hormone replacement therapy. Based on that limitation in data collection, we did not have information about use of HRT in the follow-up situation.

In conclusion, we found that type 2 diabetes was associated with accelerated muscle strength decline over 11-years of follow-up in men aged 55 years and older. Since muscle strength is a prerequisite for physical functioning, individuals with diabetes may be at greater risk of developing disabilities in mobility and functioning [5, 20]. Therefore, it is of great importance to prevent development of type 2 diabetes and among those with diabetes emphasize should be placed to adequate strength training to counteract the muscle strength decline.

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Statement of Ethics

All participants signed a written informed consent form approved by the Ethical Committee for Epidemiology and Public Health in the Hospital District of Helsinki and Uusimaa in Finland.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Figure Legend

Fig. 1. Unadjusted handgrip strength at baseline and 11-year follow-up among men and women with diabetes, pre-diabetes, non-diabetes at baseline.

Table 1. Baseline characteristics of the participants by sex and diabetes status in the Health 2000 Survey.

	MEN *(n=514)*				WOMEN *(n=676)*			
	Diabetes (*n*=43)	Pre-diabetes (*n*=82)	Non-diabetes (*n*=389)	p-value	Diabetes (*n*=39)	Pre-diabetes (*n*=77)	Non-diabetes (*n*=560)	p-value
Age, years: mean (SEM)	62.8 (1.06)	62.9 (0.70)	62.6 (0.34)	0.940	64.3 (0.96)	64.0 (0.77)	63.4 (0.27)	0.557
BMI, kg/m^2: mean (SEM)	29.6 (0.54)	29.0 (0.53)	27.1 (0.19)	<0.001	31.6 (0.71)	29.1 (0.49)	27.5 (0.19)	<0.001
Education, %				0.12				0.11
0-9 years	68.9	61.3	58.9		67.0	66.2	55.9	
10–12 years	24.2	15.9	17.8		21.3	24.6	23.8	
13 years or more	6.9	22.8	23.4		11.7	9.2	20.3	
Missing, *n*	1	0	7		0	0	6	
Hormone Replacement Therapy, %								0.03
Current user					31.6	19.7	37.0	
Former user					8.1	18.5	13.9	
Non-user					60.3	61.8	49.1	
Missing, *n*					0	0	5	
Physical Activity, %				0.29				0.29
Sedentary	24.6	20.3	14.8		26.5	28.6	20.5	
Moderate	59.1	58.6	59.7		62.7	64.8	66.4	
Very active	16.3	21.1	25.5		10.8	6.6	13.1	

Missing, *n*	0	1	8		2	1	7	
Alcohol consumption, %				0.87				0.09
Heavy user	6.8	4.9	7.2		8.6	3.9	3.6	
Moderate user	62.4	70.6	67.9		34.2	42.1	53.1	
Non-user	30.8	24.5	24.9		57.2	54.0	43.3	
Missing, *n*	0	2	6		2	2	5	
Smoking, %				0.85				0.38
Current smoker	16.3	12.7	17.1		5.2	6.6	10.7	
Ex-smoker	38.4	46.0	41.7		18.9	13.2	10.8	
Never-smoker	45.3	41.3	41.2		75.9	80.2	78.5	
Missing, *n*	0	0	2		0	0	1	
Chronic conditions, %								
Hypertension	57.6	57.7	37.0	<0.001	68.1	51.6	38.7	<0.001
Coronary heart disease	14.8	21.0	12.7	0.13	16.6	10.2	8.6	0.25
Heart failure	7.0	8.5	2.6	0.02	11.7	4.0	2.4	0.01
Osteoarthritis (knee, hip)	26.0	10.2	19.6	0.05	17.1	26.7	21.7	0.49
Inflammatory arthritis	0.0	4.9	2.5	0.30	5.0	5.4	3.9	0.80
Pulmonary diseases	7.1	17.1	13.0	0.27	25.7	9.2	16.1	0.10
Stroke	9.4	4.4	2.8	0.10	2.5	4.1	2.8	0.75
Parkinson’s disease	0.0	0.0	0.4	na	0.0	0.0	0.2	na

Chronic mental disorders	11.6	9.8	9.7	0.91	15.6	12.0	16.0	0.66
Cancer	2.3	4.7	3.9	0.79	15.8	9.1	9.4	0.43

Note: SEM= Standard Error of the mean, BMI= Body Mass Index, na= not applicable

Table 2. Changes in handgrip strength in Newtons during 11-year follow-up among men and women with diabetes, pre-diabetes and non-diabetes at baseline. Unstandardized regression coefficients (β) with their 95% confidence intervals (CI) from linear regression models.

	MEN *(n=514)*			WOMEN *(n=676)*		
	Non-diabetes (*n*=389)	Pre-diabetes (*n*=82)	Diabetes (*n*=43)	Non-diabetes (*n*=560)	Pre-diabetes (*n*=77)	Diabetes (*n*=39)
	β estimate (95% CI)			β estimate (95% CI)		
Model 1	-63.0 (-70.4 to -55.5)	-78.2 (-90.7 to -65.7)	-98.6 (-119.1 to -78.0)	-21.1 (-25.0 to -17.1)	-19.9 (-31.7 to -8.0)	-27.3 (-42.1 to -12.4)
Model 2	-64.7 (-73.6 to -55.8)	-79.2 (-93.5 to -64.9)	-97.4 (-116.6 to -78.2)	-20.8 (-25.2 to -16.3)	-16.8 (-26.9 to -6.7)	-25.7 (-38.9 to -12.4)
Model 3	-85.0 (-99.6 to -70.4)	-100.3 (-120.3 to -80.5)	-118.0 (-141.8 to -94.1)	-23.3 (-35.1 to -11.5)	-20.6 (-35.1 to -6.2)	-29.7 (-48.1 to -11.2)
Model 4	-88.9 (-125.7 to -52.1)	-101.4 (-142.4 to -60.4)	-121.1 (-164.7 to -77.5)	-39.4 (-64.4 to -14.3)	-35.5 (-62.9 to -8.1)	-48.1 (-73.8 to -22.3)
Model 5	-93.8 (-133.6 to -54.0)	-103.4 (-146.5 to -60.3)	-126.4 (-176.7 to -76.0)	-39.4 (-67.6 to -11.2)	-27.1 (-57.5 to 3.3)	-42.7 (-70.9 to -14.6)

Note:

Model 1: adjusted for muscle strength at baseline

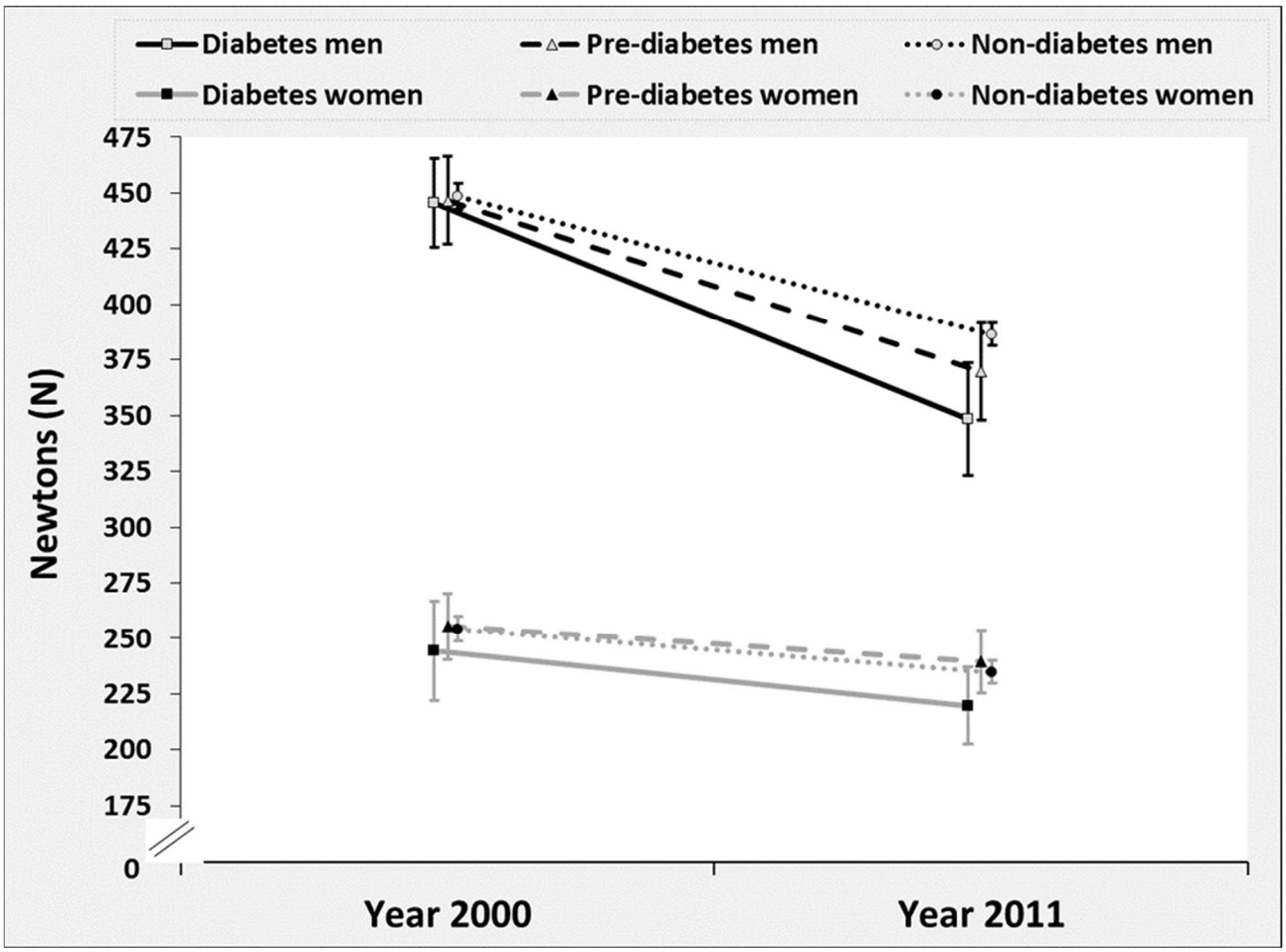
Model 2: additionally adjusted for age, education

Model 3: additionally adjusted for Body Mass Index, hormone replacement therapy (women), physical activity, smoking status, alcohol consumption

Model 4: additionally adjusted for chronic conditions

Model 5: additionally adjusted for diabetes status at follow-up

Fig. 1. Unadjusted handgrip strength at baseline and 11-year follow-up among men and women with diabetes, pre-diabetes, non-diabetes at baseline.



Supplementary Table 1. Baseline characteristics of all participants who had baseline hand grip strength measure and diabetes status in the Health 2000 Survey.

	MEN *(n*=1127*)*				WOMEN *(n*=1646)			
	Diabetic (*n*=148)	Pre-diabetic (*n*=182)	Non-diabetic (*n*=797)	p-value	Diabetic (*n*=188)	Pre-diabetic (*n*=214)	Non-diabetic (*n*=1244)	p-value
Age, years: mean (SEM)	67.7 (0.71)	66.4 (0.58)	65.8 (0.28)	0.036	72.2 (0.67)	68.9 (0.62)	67.7 (0.24)	<0.001
BMI: mean (SEM)	29.3 (0.39)	28.8 (0.34)	26.9 (0.13)	<0.001	30.4 (0.43)	29.4 (0.38)	27.4 (0.13)	<0.001
Education, %				0.58				0.001
0-9 years	72.9	69.2	67.7		79.7	75.5	66.0	
10–12 years	15.4	14.2	14.8		11.0	16.1	18.3	
13 years or more	11.7	16.6	17.5		9.3	8.5	15.7	
Missing, *n*	4	3	23		16	6	53	
HRT, %								<0.001
Current user					12.9	12.6	27.5	
Former user					7.0	15.9	12.4	
Non-user					80.1	71.5	60.1	
Missing, *n*					9	7	45	
Physical Activity, %				0.007				<0.001
Sedentary	34.1	26.6	21.7		53.9	35.7	29.1	
Moderate	53.5	58.5	57.6		39.8	58.9	60.8	
Very active	12.4	14.9	20.6		6.3	5.4	10.1	
Missing, *n*	4	7	30		15	11	64	

Alcohol consumption, %				0.30				<0.001
Heavy user	9.8	7.1	7.9		2.9	3.1	2.5	
Moderate user	50.3	61.9	59.5		21.0	33.9	42.8	
Non-user	39.9	31.0	32.6		76.1	63.0	54.7	
Missing, *n*	5	8	27		16	13	60	
Smoking, %				0.13				0.95
Current smoker	18.6	17.7	22.0		8.6	10.2	9.9	
Ex-smoker	54.7	49.3	43.9		12.4	10.1	11.7	
Never-smoker	26.7	33.0	34.1		79.0	79.7	78.4	
Missing, *n*	0	1	4		4	1	10	
Chronic conditions, %								
Hypertension	57.9	53.3	38.4	<0.001	63.6	54.9	42.7	<0.001
Coronary heart disease	27.6	26.6	20.0	0.038	27.2	18.8	13.4	<0.001
Heart failure	14.9	9.0	6.4	0.002	24.2	13.7	8.2	<0.001
Osteoarthritis (knee, hip)	24.5	17.9	20.0	0.33	28.9	30.0	25.4	0.29
Inflammatory arthritis	5.6	5.2	4.7	0.88	10.6	6.7	6.0	0.082
Pulmonary diseases	18.2	20.7	14.8	0.12	21.7	14.5	18.3	0.20
Stroke	14.7	4.4	5.7	<0.001	5.5	5.3	4.3	0.62
Parkinson’s disease	0.0	0.7	1.3	0.33	1.6	0.0	0.5	0.059
Chronic mental disorders	12.9	11.4	10.9	0.80	13.6	12.1	16.7	0.17
Cancer	5.1	8.7	6.4	0.38	14.8	9.3	11.0	0.22

Notes: SEM= Standard Error of the mean, BMI= Body Mass Index, HRT= Hormone Replacement Therapy

Supplementary Figure 1. Box plot figure of hand grip strength in Newtons (N) at baseline and 11-year follow-up among men and women in diabetes, pre-diabetes, and non-diabetes at baseline. Values are unadjusted.