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Leisure-time physical activity, occupational physical activity, and the risk of type 2 diabetes: the HUNT study

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Abstract

Background: Type 2 diabetes has become one of the major health concerns in the world, with its prevalence growing over the last decades. Previous studies have shown that leisuretime physical activity may reduce the risk of developing type 2 diabetes, and that there may be a dose-response relationship. However, not many studies have looked at the potential benefits of occupational physical activity. Therefore, the aims of our study were to investigate both leisure-time and occupational physical activity in association to risk of type 2 diabetes and how they modify each other's association in a young to middle-aged adult population. Methods: We investigated 18 734 diabetes-free participants based on data from the two latest surveys from the Nord-Trøndelag Health Study (HUNT2 and HUNT3). The association between leisure-time physical activity, occupational physical activity and risk of type 2 diabetes were explored using univariate and multivariable logistic regression analysis. Adjustments were made for sex, age, BMI, smoking status, alcohol intake per/month, education, economic difficulties, history with chronic disease and family history of diabetes. **Results:** Being moderately active in leisure-time was associated with ~30% reduced risk of developing type 2 diabetes, whereas participants being highly active in leisure-time had ~57% reduced risk, compared to being inactive or very low. Much walking at work, much walking/lifting at work and heavy physical work was not significantly associated with reduced risk for the entire population, but among participants having inactive or very low leisure-time physical activity, active work had ~40-50% reduced risk, compared to those with mostly sedentary work. In addition, participants who had mostly sedentary work, gained an extra risk reduction if they were active in their leisure-time, compared with those who were inactive or had low activity.

Conclusion: Our study supports previous findings that moderate and high levels of leisuretime physical activity reduce the risk of type 2 diabetes, and that it seems to be a doseresponse relationship. Occupational physical activity may contribute to risk reduction among individuals who are inactive in leisure-time.

Sammendrag

Bakgrunn: Type 2 diabetes har blitt et av de største helseproblemene i verden og prevalensen har økt kraftig de siste årene. Tidligere studier har vist at fysisk aktivitet på fritiden kan være med på å redusere risikoen for utviklingen av type 2 diabetes og at det muligens er et doserespons forhold. Det er dog veldig få studier som har undersøkt hvorvidt aktivitet i jobb kan ha den samme potensielle effekten. Målene med denne studien var derfor å undersøke hvordan bade aktivitet i fritiden og aktivitet i jobb påvirker risikoen for å utvikle type 2 diabetes og hvordan disse påvirker hverandre i assosiasjon til risiko for type 2 diabetes. **Metode:** Vi undersøkte 18 734 deltakere som var frie for diabetes, basert på data fra de to siste Helseundersøkelsene i Nord-Trøndelag (HUNT2 og HUNT3). Assosiasjonen mellom aktivitet på fritiden, aktivitet på jobb og risiko for type 2 diabetes ble utforsket ved hjelp av logistiske regresjonsanalyser med en og med flere variabler. Vi justerte analyser for alder, BMI, røyking, alkohol inntak per/måned, utdanning, økonomiske vanskeligheter, historikk med andre kroniske lidelser og familiehistorikk med diabetes.

Resultater: Moderat aktivitet på fritiden var assosiert med ~30% redusert risiko for å utvikle type 2 diabetes, mens høy aktivitet var assosiert med ~57% redusert risiko, sammenlignet med å være inaktiv eller ha veldig lav aktivitet på fritiden. Mye gange på jobb, mye løfting på jobb og tung fysisk jobb var ikke signifikant assosiert med redusert risiko for å utvikle type 2 diabetes for hele populasjonen, men deltakere som var inaktive eller hadde veldig lav aktivitet på fritiden i kombinasjon med aktiv jobb hadde ~40-50% redusert risiko, sammenlignet med deltakere som hadde for det meste inaktiv jobb. Deltakere som hadde inaktiv jobb, fikk ekstra redusert risiko hvis de hadde moderat og høy aktivitet i fritiden, sammenlignet med de som var inaktive eller hadde lav aktivitet.

Konklusjon: Denne studien støtter tidligere funn om at moderat og høy aktivitet på fritiden reduserer risikoen for utviklingen av type 2 diabetes og at det kan virke som et dose-respons forhold, hvor mer aktivitet gir lavere risiko. Aktivitet i jobb kan redusere risikoen for type 2 diabetes blant personer som allerede er inaktive på fritiden.

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Introduction

Diabetes has become one of the most common metabolic disorders over the last decades. Since the year 2000, the International Diabetes Federation (IDF) has published detailed estimates regarding diabetes. The latest, seventh edition suggested that 415 million people had diabetes worldwide in 2015 and that more than 300 million were at an elevated risk of developing diabetes due to impaired glucose tolerance [1]. Because of this, the prevalence was suggested to increase to more than 600 million by the year 2040 [1]. Five million deaths were linked to diabetes in 2015 and the financial costs were estimated between 5-20% of the total health expenditure of different countries, in addition to individual financial costs of insulin and other diabetes-related medicines [1]. The prevalence of diverse types of diabetes differed in countries, however, it was suggested that up to 91% of the cases were type 2 diabetes in adults [1].

Many previous studies have investigated the link between physical activity and risk of developing type 2 diabetes. A recently published meta-analysis of cohort studies suggested an inverse association between leisure-time physical activity level and risk of type 2 diabetes [2]. This study showed that moderate levels of leisure-time physical activity (150 min/week of moderate intensity) was associated with a ~26% risk reduction in comparison to inactive individuals, and that higher levels of activity was associated with further lowered risk [2]. This relationship was not linear; doubling the activity level did not seem to double the risk reduction, however, high levels of leisure-time physical activity was associated with a further ~10-15%, compared to moderate. This study suggested a potential dose-response relationship. The majority of the studies included in this systematic review investigated middle-aged to older adults (median age ~50) [3-27], with only four studies [28-31] investigating a young to middle-aged population (median age ~40). More research is therefore needed to establish understanding of the potential benefits regarding leisure-time physical activity in association with type 2 diabetes in a population of a younger age.

Only three of the previous studies [10, 14, 23] included data on occupational physical activity. In a study by Hu et al. [10], leisure-time physical activity and occupational physical activity were merged to investigate total activity level, thus making it difficult to draw any conclusions of the potential benefits from occupational physical activity in itself. In a study by Steinbrecher et al. [23], occupational physical activity was included under the category "vigorous work", which also included work at home. Because of this, there was a lack of details regarding the type or intensity of occupational physical activity in both mentioned studies, thus requiring more research to explore this association further. A recent study investigating the potential benefits of standing time at work in relation to risk of type 2 diabetes, could not prove a significant association [32]. However, this study only had 293 participants [32]. Investigations with a larger number of participants and a more detailed look at types of occupational physical activity are warranted to assess if occupational physical activity has the same benefits as leisure-time physical activity on the risk of type 2 diabetes.

We therefore aimed to investigate if leisure-time physical activity and occupational physical activity were associated with the risk of type 2 diabetes in a younger adult population, and if occupational physical activity modified the association of leisure-time physical activity with type 2 diabetes and vice versa.

Methods

Study population

We studied participants who took part in the Nord-Trøndelag Health Study (HUNT), specifically the second (HUNT2) and the third (HUNT3) surveys. The population of Nord-Trøndelag is considered as a reasonable representative of the general Norwegian people, with regard to economy, distribution of age, morbidity and mortality [33]. HUNT2 was conducted in 1995-1997 and all adults aged 19 or older who lived in Nord-Trøndelag were invited to participate [33]. A total of 65 215 people participated in HUNT2. Among these, 57% (n=37 059) also took part in HUNT3, which was conducted in 2006-2008. To establish our study cohort, participants who were free from diabetes at baseline, took part in both surveys and were aged <65 in HUNT3 were selected (n=25 282). Diabetes at baseline were defined as those who answered that they had or had had diabetes in the HUNT2 questionnaires or those who exceeded a non-fasting blood glucose measurement of >11 mmol/L from clinical testing in HUNT2. We then excluded those who had missing data regarding physical activity level in HUNT2 or missing data on diabetes from the HUNT3. The remaining 18 734 participants

constituted our analysis cohort, who were diabetes-free and aged 19-55 years at baseline (HUNT2).

Leisure-time and occupational physical activity

Information on physical activity at baseline was collected by questionnaires. There were two questions regarding leisure-time physical activity in the HUNT2 questionnaire, distinguishing between hours of light (not sweating/not out of breath) and vigorous (sweating/out of breath) activity per week. Based on previous studies [34, 35], we classified leisure-time physical activity into four different groups: "Inactive or very low", "low", moderate" and "high". The "inactive or very low" group included those who did not do any activity, or who did vigorous physical activity combined with 0-2 hours of light activity per week. "Low" was defined by doing 3 or more hours of light activity combined with no vigorous activity, or 0-2 hours of light activity combined with less than 1 hour of vigorous activity. "Moderate" was defined by doing 3 or more hours of light activity combined with less than one hour of vigorous activity, or 1-2 hours of vigorous activity regardless of the amounts of light activity. The "high" group included those who did 3 or more hours of vigorous activity, regardless of the amounts of light activity.

Levels of occupational physical activity were defined by using the original categories from the HUNT-2 questionnaire. The different categories were "mostly sedentary work", "much walking at work", "much walking or lifting at work" or "heavy physical work".

Other baseline variables

Other baseline variables were obtained through the HUNT2 questionnaires. The variables were categorized as following: sex (men, women), age (19-29, 30-39, 40-49, 50-55 years old), body mass index (BMI, kg/m²) (<25.0, 25.0-29.9 and >30.0 kg/m², smoking status (never, exsmoker and current smoker), alcohol intake per month (abstainer, 1-4 times and >5 times), education (<10 years, 10-12 years and >13 years), economic difficulties (yes/no), other chronic diseases (yes/no) and family history with diabetes (yes/no). Weight and height of the participants were measured by professionals. Economic difficulties were defined as difficulties regarding cost of either food, transport or housing. Chronic diseases were defined using the following question: "do you suffer from any long-term illness or injury of a physical

or psychological nature that impairs your functioning in your everyday life? (Long-term means at least one year)".

Diabetes

New cases of diabetes during the follow-up were defined if the participants answered that they had or had had diabetes in the HUNT3 questionnaire in combination with a diagnosis age older than the participation age in HUNT2. We also defined new cases with a non-fasting blood glucose measurement of >11 mmol/L from clinical testing in HUNT3. To ascertain type 2 diabetes, we excluded all new cases whose age at diagnosis in HUNT3 or age at clinical testing of blood glucose was less than 35 years old.

Statistical analysis

Population characteristics were obtained through descriptive statistics and were presented as number of participants (no.) and percentage (%). The association between leisure-time physical activity, occupational physical activity and risk of type 2 diabetes were explored using univariate and multivariable logistic regression analysis, which resulted in crude and adjusted odds ratios (OR) with 95% confidence intervals (95% CI). Model 1 was adjusted for sex, age, BMI, smoking status, alcohol intake per/month, education, economic difficulties, history with chronic disease and family history of diabetes. Model 2 was adjusted with all covariates from model 1, plus either leisure-time physical activity or occupational activity. To evaluate effect modification, the association of leisure-time physical activity with risk of type 2 diabetes was analyzed in different stratum of occupational activity. Similarly, the association of occupational activity with risk of type 2 diabetes was evaluated in different stratum of leisure time physical activity. Similarly, the stratum of leisure time physical activity. All analyses were conducted using IBM SPSS software (version 24 for windows; SPSS Institute, Chicago, Illinois).

Ethics

This study was approved by the Regional Committees for Medical and Health Research Ethics. All participants have been informed and signed consent forms for participating in the HUNT study.

Results

Baseline characteristics for participants in the study cohort (participants who were free from diabetes at baseline, took part in both surveys and were aged <65 years old at HUNT3) and participants in the analysis cohort (excluding participants with missing data on physical activity from HUNT2, and missing data on diabetes from HUNT3) are shown in table 1. The distribution of baseline characteristics in the two tables was similar without any major differences. For the analysis cohort (the participants we analyzed in our study), the age distribution was mainly between 30-50 years old, and the BMI of the participants were mainly <25 or 25-29.9. Approximately 1/10 had family history with diabetes. 25.7% of the participants were inactive or had very low leisure-time activity, 25.3% had low leisure-time activity, whereas 36.2% were moderately active and only 12.8% were highly active in their leisure-time. 30.4% had mostly sedentary work, 30.2% had much walking at work, 27.3% had much walking at work and only 12.1% had heavy physical work.

Baseline characteristics of the population in the analysis cohort divided into groups of leisuretime physical activity are shown in table 2. The results showed that the participants were mostly moderate active in both men and women. Women were generally more inactive than men, and there were more men (17.4%) than women (8.5%) in the high leisure-time physical activity group (3 or more hours of vigorous activity per week). There were more subjects with a BMI >30 or aged 30-55 years old in the inactive participants than in the high physical activity group, and there were more current smokers in the inactive group compared to the rest. Also, inactive participants were more likely to have had other chronic diseases, compared to the other groups.

Baseline characteristics of the population in the analysis cohort divided into groups of occupational physical activity are shown in table 3. Results showed that women generally had more walking or walking/lifting at work than men, whereas 22.2% of the men and only 2.9% of the women had heavy physical work. Participants in the age group 19-29 years old were less likely to have work that was mostly sedentary compared to the other age groups. In mostly sedentary, much walking and much walking/lifting at work, there were more participants with a BMI of <25 compared to higher BMI, however, for those having heavy physical work, a BMI of 25-29.9 was more likely. A larger part of the participants having

much walking/lifting or heavy physical work were current smokers, compared to mostly sedentary or much walking at work.

The association between leisure-time physical activity and risk of type 2 diabetes, along with analysis in the subgroups of occupational activity, is shown in table 4. For the entire population (n=18 734), low leisure-time physical activity was not significantly associated with a risk reduction in univariate analysis (OR 0.80, 95% CI 0.62-1.03). Moderate activity was associated with a 44% risk reduction (OR 0.56 95% CI 0.43-0.71) and high activity was associated with a 68% risk reduction (OR 0.32, 95% CI 0.21-0.50), compared to the inactive or very low leisure-time activity groups. After adjustments for all covariates (model 1), odds ratios were slightly increased; OR 0.88, 95% CI 0.67-1.13 for low, OR 0.71, 95% CI 0.55-0.92 for moderate and OR 0.42, 95% CI 0.27-0.67 for high, but remained significant for the two most active groups. After adjusting for all covariates plus occupational physical activity (model 2) odds ratios were nearly unchanged; OR 0.87, 95% CI 0.67-1.13 for low, OR 0.71, 95% CI 0.55-0.92 for moderate and OR 0.43, 95% CI 0.27-0.68 for high.

Odds ratios for risk of type 2 diabetes with different levels of leisure-time physical activity were strengthened after adjusting for all covariates (model 1) in the participants with mostly sedentary work; OR 0.71, 95% CI 0.47-1.08 for low, OR 0.45, 95% CI 0.28-0.71 for moderate and OR 0.28, 95% CI 0.12-0.66 for high, showing a slightly stronger risk reduction compared to the whole population. The corresponding adjusted odds ratios and 95% CIs in participants with much walking at work, with much walking or lifting or with heavy physical work did not demonstrate any statistically significant associations between leisure-time physical activity and risk of type 2 diabetes (table 4).

The association between occupational physical activity and risk of type 2 diabetes, along with the analyses in the subgroups of leisure-time physical activity is shown in table 5. Results are represented in the same way as in table 4. For the entire analysis population (n=18 734), crude odds ratios were OR 0.77, 95% CI 0.60-1.00 for much walking, OR 0.69, 95% CI 0.53-0.91 for much walking/lifting and OR 0.93, 95% CI 0.68-1.29 for heavy physical work compared to mostly sedentary work. After adjustments for all covariates (model 1), the results were no longer significant; OR 0.81, 95% CI 0.62-1.05 for much walking, OR 0.77, 95% CI 0.58-1.02 for much walking/lifting and OR 0.81, 95% CI 0.57-1.14 for heavy physical work. Additional adjustments for leisure-time physical activity (model 2) increased the odds ratios slightly OR

0.82, 95% CI 0.63-1.07 for much walking, OR 0.78, 95% CI 0.59-1.04 for much walking/lifting and OR 0.84, 95% CI 0.59-1.19 for heavy physical work and remained not significant.

However, in participants who were inactive or had very low leisure-time physical activity (n=4817), significant associations were demonstrated between occupational activity and risk of type 2 diabetes, i.e. ~50% reduced risk with much walking at work OR 0.51, 95% CI 0.32-0.81, 40% reduced risk with much walking/lifting at work OR 0.60, 95% CI 0.38-0.94 and 45% reduced risk with heavy physical work OR 0.55, 95% CI 0.30-0.99 after adjustments for all covariates (model 1). No significant associations of occupational activity with risk of type 2 diabetes were observed in the low, moderate or high leisure-time physical activity groups (table 5).

Table 1. Baseline characteristics for the study cohort and analysis cohort.

	2	2		
	Study col	nort	Analysis of	cohort
	n	%	n	%
Total	25282		18734	
Sex				
Men	11252	44.5	9010	48.1
Women	14030	55.5	9724	51.9
Age				
19-29	3988	15.8	3053	16.3
30-39	7553	29.9	5985	32.0
40-49	9796	38.7	7086	37.8
50-55	3945	15.6	2610	13.9
BMI				
<25	11656	46.1	8718	46.5
25-29.9	10462	41.4	7830	41.8
>30	3114	12.3	2152	11.5
Missing	50	0.2	34	0.2
Smoking				
Never	11494	45.5	8910	47.6
Ex-smoker	6326	25.0	4688	25.0
Current	7277	28.8	5025	26.8
Missing	185	0.7	111	0.6
Alcohol p/month				
Abstainer	6913	27.3	4735	25.3
1-4 times	14220	56.3	10874	58.0
>5 times	3398	13.4	2750	14.7
Missing	751	3.0	375	2.0
Education				
<10 years	5036	19.9	3121	16.7
10-12 years	13466	53.3	10112	54.0
>13 years	6559	25.9	5403	28.8
Missing	221	0.9	98	0.5
Economic difficulties				
Yes	7068	27.9	5095	27.2
No	14505	57.4	11040	58.9
Missing	3709	14.7	2599	13.9
Chronic disease				
Yes	4191	16.6	2823	15.1
No	20354	80.5	15549	83.0
Missing	737	2.9	362	1.9
FH diabetes				
Yes	3272	12.9	2308	12.3
No	18360	72.6	13847	73.9
Missing	3650	14.5	2579	13.8
Leisure-time PA p/week				
Inactive or very low	5335	21.1	4817	25.7
Low	5092	20.2	4731	25.3
Moderate	7287	28.8	6788	36.2
High	2629	10.4	2398	12.8
Missing	4939	19.5	0	0
Occupational PA p/week				
Mostly sedentary work	6890	27.3	5694	30.4
Much walking	7229	28.6	5652	30.2
Much walking or lifting	6619	26.2	5109	27.3
Heavy physical work	2843	11.2	2279	12,1
Missing	1701	6.7	0	0

BMI, body mass index, FH diabetes, family history with diabetes, Chronic disease, history with chronic diseases other than diabetes, PA, physical activity. m, number of participants, %, row percentage.

Table 2. Baseline characteristics for the participants divided into groups of leisure-time physical activity.

	Inactive		Low	Low		Moderate		<u>High</u>	
	n	%	n	%	n	%	n	%	p-value
Sex									
Men	2060	22.9	2199	24.4	3182	35.3	1569	17.4	< 0.001
Women	2757	28.4	2532	26	3606	37.1	829	8.5	
Age									
19-29	657	21.5	688	22.5	1138	37.3	570	18.7	< 0.001
30-39	1535	25.6	1470	24.6	2272	38	708	11.8	
40-49	1882	26.5	1870	26.4	2507	35.4	827	11.7	
50-55	743	28.5	703	26.9	871	33.4	293	11.2	
BMI	715	20.0	105	20.9	0,1	55.1	2,5	11.2	
<25	2066	23.7	2097	24	3309	38.0	1246	14.3	< 0.001
25-29,9	2000	26	2097	24 25.9	2820	36.0	952	14.5	<0.001
>30		20 33							
	710		599	27.8	644	29.9	199	9.3	
Missing	8	23.5	10	29.4	15	44.1	1	3	
Smoking									
Never	1965	22.1	2157	24.2	3431	38.5	1357	15.2	< 0.001
Ex-smoker	1184	25.3	1232	26.3	1685	35.9	587	12.5	
Current	1642	32.7	1318	26.2	1625	32.3	440	8.8	
Missing	26	23.4	24	21.6	47	42.4	14	12.6	
Alcohol p/ month									
Abstainer	1474	31.1	1254	26.5	1496	31.6	511	10.8	< 0.001
1-4 times	2648	24.3	2700	24.8	4095	37.7	1431	13.2	
>5 times	590	21.5	686	24.9	1067	38.8	407	14.8	
Missing	105	28	91	24.3	130	34.7	49	13	
Education <10 years	1106	35.5	828	26.5	831	26.6	356	11.4	< 0.001
10-12 years	2709	26.8	828 2563	20.3 25.4	3563	20.0 35.2	1277	11.4	<0.001
>13 years	971	18	1314	24.3	2369	43.8	749	13.9	
Missing	31	31.7	26	26.5	25	25.5	16	16.3	
Economic									
difficulties									
Yes	1401	27.5	1326	26	1795	35.2	573	11.3	< 0.001
No	2680	24.3	2804	25.4	4109	37.2	1447	13.1	
Missing	736	28.3	601	23.1	884	34	378	14.6	
Chronic Disease	0.65	20.6	704	24.0	016	22.5	220	10	0.001
Yes	865	30.6	704	24.9	916	32.5	338	12	< 0.001
No	3857	24.8 26.2	3943 84	25.4	5737 125	36.9 27.2	2012	12.9	
Missing FH Diabetes	95	26.2	84	23.2	135	37.3	48	13.3	
Yes	626	27.1	626	27.1	807	35	249	10.8	0.007
No	3450	27.1 24.9	3513	27.1 25.4	807 5707	35 36.9	249 1777	10.8	0.007
Missing	5450 741	24.9 28.7	5515 592	23.4 23	3707 874	30.9 33.9	372	12.8 14.4	

BMI, body mass index, FH diabetes, family history with diabetes, Chronic disease, history with chronic diseases other than diabetes. n, number of participants, %, row percentage.

	Mostly sedentary work		Much walking at work		Much walking or lifting at work		<u>Heavy physical</u> <u>work</u>		
_	n	%	n	%	n	%	n	%	p-value
Sex									
Men	2920	32.4	2125	23.6	1967	21.8	1998	22.2	< 0.001
Women	2774	28.5	3527	36.3	3142	32.3	281	2.9	
Age									
19-29	730	23.9	877	28.7	1031	33.8	415	13.6	< 0.001
30-39	1698	28.4	1713	28.6	1784	29.8	790	13.0	
40-49									
50-55	2414	34.1	2190	30.9	1742	24.6	740	10.4	
BMI	852	32.6	872	33.4	552	21.2	334	12.8	
<25	2601	29.8	2742	31.5	2477	28.4	898	10.3	0.003
25-29,9	2451	31.3	2265	28.9	2046	26.1	1068	13.7	
>30	630	29.3	637	29.6	575	26.7	310	14.4	
Missing	12	35.3	8	23.5	11	32.4	3	8.8	
Smoking									
Never	2783	31.2	2744	30.8	2197	24.7	1186	13.3	< 0.001
Ex-smoker	1522	32.5	1369	29.2	1272	27.1	525	11.2	101001
Current	1322	27.2	1504	29.9	1598	31.8	525	11.2	
Missing	22	19.8	1304 35	29.9 31.5	42	31.8	12	10.8	
Alcohol p/ month	22	17.0	55	51.5	72	51.7	12	10.0	
Abstainer	1172	24.7	1509	31.9	1466	31	588	12.4	< 0.001
1-4 times	3301	30.3	3248	29.9	2958	27.2	1367	12.6	
>5 times	1118	40.7	779	28.3	560	20.4	293	10.6	
Missing	103	27.5	116	30.9	125	33.3	31	8.3	
Education									
<10 years	572	18.3	1020	32.7	956	30.6	573	18.4	< 0.001
10-12 years	2701	26.7	2716	26.9	3165	31.3	1530	15.1	
>13 years	2395	44.3	1893	35	953	17.7	162	3	
Missing	26	26.5	23	23.5	35	35.7	14	14.3	
Economic difficulties									
Yes	1301	25.5	1574	30.9	1625	31.9	595	11.7	< 0.001
No	3645	33	3317	30.1	2772	25.1	1306	11.8	
Missing	748	28.8	761	29.3	712	27.4	378	14.5	
Chronic Disease									
Yes	875	31	842	29.8	719	25.5	387	13.7	0.166
No	4725	30.4	4698	30.2	4281	27.5	1845	11.9	
Missing	94	26	112	30.9	109	30.1	47	13	
FH Diabetes									
Yes	689	29.9	738	32	608	26.3	273	11.8	< 0.001
No Missing	4267	30.8	4163	30.1	3792	27.4	1625	11.7	
Missing	738	28.6	751	29.1	709	27.5	381	14.8	

Table 3. Baseline characteristics for the participants divided into groups of occupational physical activity.

BMI, body mass index, FH diabetes, family history with diabetes, Chronic disease, history with chronic diseases other than diabetes. n, number of participants, %, row percentage.

Table 4. Leisure-time physical activity and risk of type 2 diabetes.

Leisure-time PA	No.	New cases	%	Crude OR (95% CI)	Adjusted OR (95% CI) Model 1ª	Adjusted OR (95% CI) Model 2 ^b
Inactive or very low	4817	140	2.9	1.00	1.00	1.00
Low	4731	111	2.3	0.80 (0.62-1.03)	0.88 (0.67-1.13)	0.87 (0.67-1.13)
Moderate	6788	111	1.6	0.56 (0.43-0.71)	0.71 (0.55-0.92)	0.71 (0.55-0.92)
High	2398	23	1	0.32 (0.21-0.50)	0.42 (0.27-0.67)	0.43 (0.27-0.68)
Mostly sedentary work. To	otal (n=5694	4)				
Leisure-time PA						
Inactive or very low	1441	62	4.3	1.00	1.00	
Low	1431	41	2.9	0.66 (0.44-0.98)	0.71 (0.47-1.08)	
Moderate	2148	30	1.4	0,32 (0.20-0.49)	0.45 (0.28-0.71)	
High	674	6	0.9	0.20 (0.09-0.46)	0.28 (0.12-0.66)	
Much walking at work. To	otal (n=5652	2)				
Leisure-time PA						
Inactive or very low	1430	30	2.1	1.00	1.00	
Low	1471	31	2.1	1.01 (0.61-1.67)	1.06 (0.63-1.78)	
Moderate	2123	40	1.9	0.90 (0.56-1.45)	1.05 (0.64-1.72)	
High	628	6	1	0.45 (0.19-1.09)	0.61 (0.25-1.51)	
Much walking or lifting at	t work. Tota	l (n=5109)				
Leisure-time PA						
Inactive or very low	1363	32	2.3	1.00	1.00	
Low	1339	21	1.6	0.66 (0.38-1.16)	0.74 (0.42-1.30)	
Moderate	1834	29	1.6	0.67 (0.40-1.11)	0.86 (0.51-1.44)	
High	573	5	0.9	0.37 (0.14-0.94)	0.51 (0.19-1.34)	
Heavy physical work. Tot	al (n=2279)					
Leisure-time PA						
Inactive or very low	583	16	2.7	1.00	1.00	
Low	490	18	3.7	1.35 (0.68-2.68)	1.60 (0.78-3.27)	
Moderate	683	12	1.8	0.63 (0.30-1.35)	0.81 (0.37-1.78)	
High	523	6	1.1	0.41 (0.16-1.06)	0.50 (0.19-1.33)	

Analysis population. Total (n=18734)

The association of various levels of leisure-time physical activity with incidence of type 2 diabetes over the 11 years of follow-up of the HUNT-study. ^a: adjusted for sex, age, BMI, smoking, alcohol intake p/month, education, economic difficulties, other chronic diseases and family history with diabetes. ^b: Adjusted for all covariates in model 1^a, plus occupational physical activity.

Table 5. Occupational physical activity and risk of type 2 diabetes.

Occupational PA	No.	New cases	%	Crude OR (95% CI)	Adjusted OR (95% CI) Model 1	Adjusted OR (95% CI) Model 2
Mostly sedentary	5694	139	2.4	1.00	1.00	1.00
Much walking	5652	107	1.9	0.77 (0.60-1.00)	0.81 (0.62-1.05)	0.82 (0.63-1.07)
Much walking/lifting	5109	87	1.7	0.69 (0.53-0.91)	0.77 (0.58-1.02)	0.78 (0.59-1.04)
Heavy physical work	2279	52	2,3	0.93 (0.68-1.29)	0.81 (0.57-1.14)	0.84 (0.59-1.19)
Inactive or very low. Total ((n=4817)					
Occupational PA						
Mostly sedentary	1441	62	4.3	1.00	1.00	
Much walking	1430	30	2.1	0.48 (0.31-0.74)	0.51 (0.32-0.81)	
Much walking/lifting	1363	32	2.3	0.54 (0.35-0.83)	0.60 (0.38-0.94)	
Heavy physical work	583	16	2.7	0.63 (0.36-1.10)	0.55 (0.30-0.99)	
Low. Total (n=4731)						
Occupational PA						
Mostly sedentary	1431	41	2.9	1.00	1.00	
Much walking	1471	31	2.1	0.73 (0.46-1.17)	0.79 (0.48-1.29)	
Much walking/lifting	1339	21	1.6	0.54 (0.32-0.92)	0.60 (0.34-1.04)	
Heavy physical work	490	18	3.7	1.29 (0.74-2.27)	1.22 (0.66-2.24)	
Moderate. Total (n=6788)						
Occupational PA						
Mostly sedentary	2148	30	1.4	1.00	1.00	
Much walking	2123	40	1.9	1.36 (0.84-2,19)	1.38 (0,84-2,27)	
Much walking/lifting	1834	29	1.6	1.13 (0,68-1,90)	1.30 (0,75-2,25)	
Heavy physical work	683	12	1.8	1.26 (0,64-2,48)	1.04 (0,51-2,13)	
High. Total (n=2398)						
Occupational PA						
Mostly sedentary	674	6	0.9	1.00	1.00	
Much walking	628	6	1	1.07 (0.35-3.35)	1.42 (0.43-4.66)	
Much walking/lifting	573	5	0.9	0.98 (0.30-3.23)	1.57 (0.41-6.06)	
Heavy physical work	523	6	1.1	1.29 (0.41-4.03)	1.32 (0.36-4.84)	

Analysis population. Total (n=18734)

The association of various levels of occupational physical activity with incidence of type 2 diabetes over the 11 years of follow-up of the HUNT-study. ^a: adjusted for sex, age, BMI, smoking, alcohol intake p/month, education, economic difficulties, other chronic diseases and family history with diabetes. ^b: Adjusted for all covariates in model 1^a, plus occupational physical activity.

Discussion

Main findings

In this longintudinal population-based study, we found that being moderate active in leisuretime was associated with a ~30% lowered risk of developing type 2 diabetes for the entire population, compared to being inactive or very low. Participants being highly active in their leisure-time had a ~57% risk reduction, showing that higher amounts of leisure-time physical activity were associated with further risk reduction. For the entire population, much walking at work, much walking/lifting at work and heavy physical work were not significantly associated with a lowered risk compared to mostly sedentary work after adjustments for all covariates. However, among participants who were inactive or very low in their leisure-time, either much walking, much walking/lifting or heavy physical work, had a ~40-50% risk reduction, compared to those with mostly sedentary work. Also, moderate to high leisure-time physical activity seemed to provide extra benefits among participants being mostly sedentary at work compared with participants having more active work.

Comparison to existing literature

Our findings on leisure-time physical activity were similar to the findings presented in the systematic review by Smith et al; i.e. moderate level of leisure-time physical activity (150 hours per/week of low to moderate intensity) was associated with a ~26% risk reduction on average [2], which is comparable to the ~30% reduced risk we found. Our results indicated a higher benefit of high leisure-time activity compared to Smith's results, however, our study did not use MMET hours/per week, thus making our study less accurate and less comparable when it comes to specific levels of leisure-time physical activity. We did however find results supporting the potential inverse dose-response relationship between leisure-time physical activity and risk of type 2 diabetes. Several studies found significant results with low levels of leisure-time physical activity similar to the "low" group in our study (3 or more hours of light activity, or 0-2 hours of light activity combined with less than 1 hour of vigorous activity) [5, 8, 14], however the majority of the studies included in Smith's review [2] showed a minimum beneficial level comparable to the "moderate" leisure-time activity level in our study. More research is therefore needed to see if low levels of leisure-time physical activity or other daily

life activities of similarly low intensity can have beneficial effects on reducing the risk of type 2 diabetes.

Villegas et al. explored the potential benefits of occupational physical activity in association to risk of type 2 diabetes [14], however, similar to our findings, they did not find any significant results for the entire population. A study investigating standing time at work in association with risk of type 2 diabetes did not find any significant association either [32]. However, Villegas et al [14] also explored if cycling or walking to work was associated with a lowered risk, and they found a significant ~15% risk reduction if the travel time was longer than 30 minutes/day. This is an interesting aspect of low leisure-time physical activity and should be further researched.

Our study differs from existing literature in that it has a slight younger population compared to most of the previous studies, and that it investigated the potential benefits of occupational physical activity in regard to risk of type 2 diabetes.

Potential biological mechanisms

There are a few biological mechanisms that could explain an inverse association between physical activity and the risk of type 2 diabetes. It is well known that physical activity improves energy balance in the body and reduces adiposity [38], which was suggested as the main risk factor for type 2 diabetes [39]. This might explain why there may be a doseresponse relationship between the two, as a higher activity level would result in a better energy balance as well as reduced risk of adiposity. Also, it is known that physical activity increases the glucose-uptake and that this effect may last for up to 2 days [40]. It is suggested that this effect increases with training volume [40], which also supports the theory of a potential dose-response relationship. Because of this, physical activity may increase the chance of keeping a low and stable blood-glucose level in the body over a period, thus resulting in a lowered risk of developing type 2 diabetes. This could also explain why occupational activity only seemed to benefit those who were inactive in their leisure-time. Since inactivity over time might result in an elevated blood glucose level, the extra physical activity through work is potentially sufficient to stabilize a low blood glucose level, as well as reducing the risk of adiposity. Vice versa, for those having mostly sedentary work, moderate and high levels of activity in leisure-time seems to benefit extra with regard to risk of type 2 diabetes.

Implications

Our results have some potential implications for public health. The Norwegian Directorate of Health have suggested that adults should be physically active at least 150 minutes a week (with low intensity) or 75 minutes a week (with high intensity) to increase the general health gain [37]. The activity levels in these recommendations are similar to the "moderate" leisure-time activity group in our study, which has shown to be protective against type 2 diabetes. Therefore, the physical activity levels suggested in the guidelines seems to be the right level of physical activity for potential reduction in risk of type 2 diabetes. However, our results suggest extra benefits if the activity level is increased beyond the recommendations. There are also no information regarding the potential benefits of occupational physical activity regarding risk of type 2 diabetes, which our study has shown to potentially be beneficial if the leisure-time activity is inactive or very low. Also, our results suggest a larger benefit for moderate and high levels of leisure-time physical activity, for those being mostly sedentary at work.

Strengths and limitations

There were several strengths of this study. It had a long follow-up period of 11 years and many participants compared to other similar studies. We had a wide age range varying from 19 to 55 years old at baseline, including both young to middle-aged participants. Baseline characteristics were similar between the study cohort and the analysis cohort, making our study a good representation of the general population, as well as reducing the potential of selection bias. This is also one of the few studies exploring the potential benefit of occupational physical activity on onset of type 2 diabetes and the first study looking at how occupational- and leisure-time activity modifies each other's association with the risk of type 2 diabetes.

There were also several limitations. There was no objective measurement of physical activity which may have caused misclassification. Participants may have been more active than our highest activity group for leisure-time physical activity. Recall-bias may have accrued, as participants had to remember how active they had been over the last year. The questionnaire did not differentiate between type-1 and type 2 diabetes, which made it likely that some of the new cases were type-1, even though ~90% of the diabetes cases in Norway are type 2 [36].

However, we think that excluding new cases under the age of 35 is a reasonable adjustment to potentially exclude cases of type-1 diabetes, as type-1 often is seen in a younger age-group [36]. It was also very likely that some participants had type 2 diabetes, but were underdiagnosed. A previous study by Stene et al. suggested that the number of people in Norway with type 2 diabetes could be 50-100% higher than the number of diagnosed people, meaning that up to half of the cases could be underdiagnosed [36]. If all cases were diagnosed, the statistical power of our results would have been improved, as the estimates would have been more precise. This could potentially have influenced our results, making the association between occupational physical activity and risk of type 2 diabetes for the entire population significant.

Even though we adjusted for a number of potential variables related to lifestyle, such as BMI, alcohol intake and smoking, we did not have any data on total energy intake or specific food intake, which has previously been shown to be related risk factors of type 2 diabetes [39]. Also, residual confounding of other variables may have occurred.

Conclusion

In conclusion, our results suggested an inverse and dose-response association between leisuretime physical activity and risk of type 2 diabetes in a general population, and further risk reduction was observed in participants being mostly sedentary at work. Much walking at work, much lifting at work and heavy physical work showed a ~40-50% lowered risk among participants who were inactive or had very low leisure-time physical activity. These results support the Norwegian public health guidelines on physical activity. Future studies should continue exploring the association between occupational physical activity and risk of type 2 diabetes in the general population, with a more detailed investigation on the actual activity level.

References

1. Diabetes Atlas. 7th edition. Brussels, Belgium: International Diabetes Federation; 2015.

2. Smith D. Andrea, Crippa A, Woodcock J, Brage S. Physical activity and incident type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of prospective cohort studies. Diabetologia 2016; 59; 2527-2545.

3. Helmrich SP, Ragland DR, Leung RW, Paffenbarger RS (1991) Physical activity and reduced occurrence of non-insulindependent diabetes mellitus. N Engl J Med 325:147–152

4. Burchfiel CM, Sharp DS et al (1995) Physical activity and incidence of diabetes: the Honolulu Heart Program. Am J Epidemiol 141:360–368

5. Lynch J, Helmrich SP, Lakka TA et al (1996) Moderately intense physical activities and high levels of cardiorespiratory fitness reduce the risk of non-insulin-dependent diabetes mellitus in middle-aged men. Arch Intern Med 156:1307–1314

6. Haapanen N, Miilunpalo S, Vuori I, Oja P, Pasanen M (1997) Association of leisure time physical activity with the risk of coronary heart disease, hypertension and diabetes in middleaged men and women. Int J Epidemiol 26:739–747

7. Folsom AR, Kushi LH, Hong CP (2000) Physical activity and incident diabetes mellitus in postmenopausal women. Am J Public Health 90:134–138

8. Okada K, Hayashi T, Tsumura K, Suematsu C, Endo G, Fujii S (2000) Leisure-time physical activity at weekends and the risk of Type 2 diabetes mellitus in Japanese men: the Osaka Health Survey. Diabet Med 17:53–58

9. Wannamethee SG, Shaper AG, Alberti KG (2000) Physical activity, metabolic factors, and the incidence of coronary heart disease and type 2 diabetes. Arch Intern Med 160:2108–2116 10. Hu G, Lindström J, Valle TT et al (2004) Physical activity, body mass index, and risk of type 2 diabetes in patients with normal or impaired glucose regulation. Arch Intern Med 164:892–896

 Nakanishi N, Takatorige T, Suzuki K (2004) Daily life activity and risk of developing impaired fasting glucose or type 2 diabetes in middle-aged Japanese men. Diabetologia 47:1768–1775

12. Weinstein AR, Sesso HD, Lee IM et al (2004) Relationship of physical activity vs body mass index with type 2 diabetes in women. JAMA 292:1188–1194

13. Hsia J, Wu L, Allen C et al (2005) Physical activity and diabetes risk in postmenopausal women. Am J Prev Med 28:19–25

14. Villegas R, Shu X-O, Li H et al (2006) Physical activity and the incidence of type 2 diabetes in the Shanghai women's health study. Int J Epidemiol 35:1553–1562

15. Magliano DJ, Barr ELM, Zimmet PZ et al (2008) Glucose indices, health behaviors, and incidence of diabetes in Australia: the Australian Diabetes, Obesity and Lifestyle Study. Diabetes Care 31:267–272

16. Chien K-L, Chen M-F, Hsu H-C, Su T-C, Lee Y-T (2009) Sports activity and risk of type2 diabetes in Chinese. Diabetes Res Clin Pract 84:311–318

17. Fretts AM, Howard BV, Kriska AM et al (2009) Physical activity and incident diabetes in American Indians: the Strong Heart Study. Am J Epidemiol 170:632–639

18. Siegel LC, Sesso HD, Bowman TS, Lee I-M, Manson JE, Gaziano JM (2009) Physical activity, body mass index, and diabetes risk in men: a prospective study. Am J Med 122:1115–1121

19. Demakakos P, Hamer M, Stamatakis E, Steptoe A (2010) Lowintensity physical activity is associated with reduced risk of incident type 2 diabetes in older adults: evidence from the English Longitudinal Study of Ageing. Diabetologia 53:1877–1885

20. Ekelund U, Palla L, Brage S et al (2012) Physical activity reduces the risk of incident type 2 diabetes in general and in abdominally lean and obese men and women: the EPIC-InterAct Study. Diabetologia 55:1944–1952

21. Grøntved A, Rimm EB, Willett WC, Andersen LB, Hu FB (2012) A prospective study of weight training and risk of type 2 diabetes mellitus in men. Arch Intern Med 172:1306–1312
22. Lee D, Park I, Jun T-W et al (2012) Physical activity and body mass index and their associations with the development of type 2 diabetes in Korean men. Am J Epidemiol 176:43–51

23. Steinbrecher A, Erber E, Grandinetti A, Nigg C, Kolonel LN, Maskarinec G (2012) Physical activity and risk of type 2 diabetes among Native Hawaiians, Japanese Americans, and Caucasians: the Multiethnic Cohort. J Phys Act Health 9:634–641

24. Shi L, Shu X-O, Li H et al (2013) Physical activity, smoking, and alcohol consumption in association with incidence of type 2 diabetes among middle-aged and elderly Chinese men. PLoS One 8, e77919

25. Fan S, Chen J, Huang J et al (2014) Physical activity level and incident type 2 diabetes among Chinese adults. Med Sci Sports Exerc 47:751–756

26. Grøntved A, Pan A, Mekary RA et al (2014) Muscle-strengthening and conditioning activities and risk of type 2 diabetes: a prospective study in two cohorts of US women. PLoS Med Publ Libr Sci 11, e1001587

27. Ding D, Chong S, Jalaludin B, Comino E, Bauman AE (2015) Risk factors of incident type 2-diabetes mellitus over a 3-year follow-up: results from a large Australian sample. Diabetes Res Clin Pract 108: 306–315

28. James SA, Jamjoum L, Raghunathan TE, Strogatz DS, Furth ED, Khazanie PG (1998)Physical activity and NIDDM in African-Americans. The Pitt County Study. Diabetes Care21:555–562

29. Meisinger C, Löwel H, Thorand B, Döring A (2005) Leisure time physical activity and the risk of type 2 diabetes in men and women from the general population. The MONICA/KORA Augsburg Cohort Study. Diabetologia 48:27–34

30. Carlsson S, Midthjell K, Tesfamarian MY, Grill V (2007) Age, overweight and physical inactivity increase the risk of latent autoimmune diabetes in adults: results from the Nord-Trøndelag health study. Diabetologia 5:55–58

31. Krishnan S, Rosenberg L, Palmer JR (2009) Physical activity and television watching in relation to risk of type 2 diabetes: the Black Women's Health Study. Am J Epidemiol 169:428–434

32. Chaput JP, Saunders TJ, Tremblay MS, Katzmarzyk PT, Tremblay A, Bouchard C. Workplace standing time and the incidence of obesity and type 2 diabetes: a longitudinal study in adults. BMC Public Health. 2015;10:15-111

33. Holmen J, Midthjell K, Krüger Ø et al. The Nord-Trøndelag Health Study 1995-1997
(HUNT 2): objectives, contents, methods and participations. Norsk Epidemiol 2003; 13: 19-3
34. Brumpton BM, Langhammer A, Ferreira MA, Chen Y, Mai XM. Physical activity and

incident asthma in adults: the HUNT study, Norway. BMJ open 2016; 6 (11):e013856.

35. Brumpton BM, Langhammer A, Henriksen AH, Camargo CA jr, Chen Y, Romunstad PR, Mai XM. Physical activity and lung function decline in adults with asthma: The HUNT Study. Respirology 2017; 2:278-283.

36. Stene LC, Midthjell K, Jenum AK, Skeie S, Birkeland KI, Lund E, Joner G, Tell GS, & Schirmer H (2004): Hvor mange har diabetes mellitus i Norge? Tidsskr Nor Lægeforen 124, 1511-1514.

37. Bahr R et al. 2009. Aktivitetshåndboken. Fysisk aktivitet I forebygging og behandling.Oslo: Helsedirektoratet

38. Mozaffarin D, Hao T, Rimm EB, Willett WC, Hu FB. Changes in diet and lifestyle and long-term weight gain in women and men. N Engl J Med. 2011; 364 (25): 2392-2404.
39. Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, Willett WC. Diet, lifestyle and the risk of type-2 diabetes in women. N Engl J Med. 2001; 345 (11):790-797.
40. Balkau B et al. Physical activity and insulin sensitivity. The RISC Study. Diabetes.
2008;57 (10): 2613-2618.