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by Ervasti J, Virtanen M, Lallukka T, Pentti J, Kjeldgård L, Mittendorfer-Rutz E, Tinghög P, Alexanderson K

Due to high prevalence of comorbid conditions related to diabetes, prevention of permanent working capacity is important. This is the first study to explore the risk of all-cause and cause-specific disability pension among people with diabetes and compare it to that of individuals without diabetes, while taking into account the competing risks and the timing of comorbid conditions.

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Key terms: cardiovascular disease; cohort study; comorbid condition; diabetes; disability; disability pension; early retirement; hypertension; ill health; mental disorder; musculoskeletal disorder; prospective study; register data; Sweden

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Contribution of comorbid conditions to the association between diabetes and disability pensions: a population-based nationwide cohort study

Jenni Ervasti, PhD,[1] Marianna Virtanen, PhD,[1] Tea Lallukka, PhD,[1, 2] Jaana Pentti, BSc,[1] Linnea Kjeldgård, MSc,[3] Ellenor Mittendorfer-Rutz, PhD,[3] Petter Tinghög, PhD,[3] Kristina Alexanderson, PhD [3]

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Objectives Using Swedish population-based register data, we examined the extent to which comorbid conditions contribute to the risk of disability pension among people with diabetes.

Methods We carried out Cox proportional hazard analyses with comorbid conditions as time-dependent covariates among 14 198 people with newly diagnosed diabetes in 2006, and 39 204 people free from diabetes during the follow-up from 2007–2010. The average follow-up times were 46 and 48 months for those with and without diabetes, respectively.

Results For those with diabetes only, the incidence of all-cause disability pension was 9.5 per 1000 person-years. The highest incidence of disability pension were for those with: diabetes and depression (23.6); diabetes and musculoskeletal disorder (30.6), and those with diabetes and more than one comorbid condition (36.5). The incidence rate was 5.8 for those without diabetes. Diabetes was associated with a 2.30 times [95% confidence interval (95% CI) 2.09–2.54] higher risk of disability pension (adjusted for sociodemographic factors). This association attenuated by 41% after further adjustment for comorbid chronic conditions. While diabetes was a risk factor for disability pension due to musculoskeletal disorders and diseases of the circulatory system, even after accounting for the above-mentioned conditions, the association between disability pension due to mental disorders and diabetes was diluted after adjustment for mental disorders.

Conclusions Although diabetes is an independent risk factor for disability pension, comorbid conditions contribute to this risk to a large degree.

Key terms cardiovascular disease; early retirement; hypertension; ill health; mental disorder; musculoskeletal disorder; prospective study; register data; Sweden.

Type 2 diabetes constitutes a considerable burden in Western countries, increasingly also in Latin America, the Caribbean, Southeast Asia, East Asia, and Oceania (1). Diabetes-related disability and the loss of healthy life-years also have a major impact from an economic point of view. While diabetes as the diagnosis on sick leave certificates is rare, individuals with diabetes have about 17 more days of absence from work due to mental disorders than individuals without diabetes. For musculoskeletal disorders and diseases of the circulatory system, the number of annual excess days of absence were 12 and 6, respectively (2). Thus, while preventing or delaying diabetes (ie, primary prevention) is the best way to avoid morbidity and premature mortality (3, 4) – due to the high prevalence of comorbid conditions related to diabetes – secondary prevention and prevention of permanent loss of working capacity are both of importance.

A systematic review concluded that diabetes was associated with a 30–300% increased risk of early retirement (5). However, most studies included in this review did not take into account comorbid conditions either at baseline or during follow-up. A few earlier studies on the

[1] Finnish Institute of Occupational Health, Helsinki, Finland.
[2] Department of Public Health, University of Helsinki, Helsinki, Finland.
[3] Division of Insurance Medicine, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden.

Corresponding author: Jenni Ervasti, Finnish Institute of Occupational Health, PO Box 40, FI-00251 Helsinki, Finland. [Email: jenni.ervasti@ttl.fi]

effect of comorbidity on work disability among people with diabetes suggest that the risk seems to be shaped by comorbid conditions (6–8). However, no previous study has examined the contribution of time-dependent comorbid conditions, ie, those that occur during follow-up, to the association between diabetes and work disability pension. Because of these shortcomings, the effect of diabetes on disability pension remains unknown.

The purpose of this study was to explore the risk of all-cause and cause-specific disability pension among people with diabetes and compare it to that of individuals without diabetes, while taking into account the timing of comorbid conditions. The specific study questions were: (i) What is the incidence and relative risk of disability pension among people with diabetes compared to those without diabetes? (ii) What is the contribution of time-dependent comorbid conditions to the risk of all-cause and diagnosis-specific disability pension among people with diabetes compared to those without diabetes having the corresponding other conditions?

Methods

We conducted a prospective study with a four-year follow-up. The data were from the nationwide population-based Insurance Medicine All-Sweden (IMAS) research database covering all people living in Sweden, from which we drew individuals aged 25–59 years (31 December 2005) living in Sweden on 31 December 2002 (N=4 123 104) (8–11). The cohort of people with diabetes consisted of all individuals with newly diagnosed diabetes during 2006, who were alive and living in Sweden in 2007 and not on disability pension during the turn of 2006/2007 (N=14 198). The follow-up was from 1 January 2007 to 31 December 2010. We set the maximum age at the end of follow-up as 64 years as 65 is the retirement age in Sweden. The data were retrieved from nationwide Swedish registers and linked using the personal identity number unique to each resident of Sweden. The following register data sources were used: (i) Statistics Sweden: Longitudinal Integration Database for Health Insurance and Labor Market Studies (LISA) regarding gender, age, education, family situation, place of birth (Sweden/not Sweden), type of living area (large city/ medium sized municipalities/ small municipalities) on 31 December 2005, and year of emigration. As we only had the year and no exact date of emigration, the date was set to 1 January each year. (ii) National Board of Health and Welfare: a) International Classification of Diseases (ICD-10)-coded (12) diagnosis-specific data on hospitalizations or specialized out-patient care during 1 January 2003–31 December 2010; b) Swedish Prescribed Drug Register: medication purchases from 1 July 2005 to 31 December 2010; c) Death register from 1 January 2003 to 31 December 2010.

National Social Insurance Agency: dates of all-cause and diagnosis-specific disability pensions from 1 January 2007 to 31 December 2010.

Comparisons to the general population were made on the basis of a 1% random sample of the population, totaling 39 204 individuals who were living in Sweden on 31 December 2006 and had no indication of diabetes during 2003–2010. The Regional Ethical Review Board, Stockholm, Sweden, approved the project.

Measures

Diabetes. Identification of diabetes was based on having at least one of the following: (i) insulin or other diabetes medication [Anatomical Therapeutic Chemical (ATC) code A10] (13); (ii) in- or out-patient record with ICD-10 code E10, E11, E12, E13, or E14 as described previously (2, 8). Of those identified as having diabetes, 7% were treated with both A10A (insulin) and A10B (other diabetes medication), 11% with A10A only, 67% with A10B only, and 15% none of these (diabetes diagnosis was based on hospital records only). In the diabetes cohort, we excluded those with an indication of diabetes during 2003–2005, and included those with an indication of diabetes during 1 January 2006–31 December 2006. The reference groups were chosen from among those with no indication of diabetes in any of the included registers during 2003–2010.

Disability pension. Data regarding the dates (first occurrence) of all-cause and diagnosis-specific (ICD-10) disability pensions were retrieved from the Social Insurance Agency, over the period of 1 January 2007 to 31 December 2010. With regard to diagnosis-specific analyses, we examined disability pensions due to mental disorders (F00-F99), musculoskeletal disorders (M00-M99), and diseases of the circulatory system (I00-I99).

Time-dependent covariates. Comorbid conditions examined were depression, other psychiatric disorders, cardiovascular disease, hypertension, and musculoskeletal disorders. These conditions are common causes of work disability in Sweden (14), and depression (15,16), cardiovascular diseases (17), and musculoskeletal disorders (18,19), have also been linked with diabetes. Indication of these conditions was based on having either a medication purchase record entry or in- or out-patient hospitalization record entry, or both. The identification of these disorders and data sources are further described in supplementary table A (www.sjweh.fi/data_repository.php). The presence or incidence of comorbid conditions among people with diabetes is likely to influence the

risk of disability pension. The presence or incidence of an illness influences the risk of disability pension also among the general population (20). Thus, information regarding the year of the first indication of an illness (pre-existing at the beginning of the follow-up or incident cases thereafter) was used as a time-dependent covariate. The timing of these conditions was calculated as either being present already at the beginning of the follow-up in 2007, incidence in 2008, incidence in 2009, or incidence in 2010. As we only had the year of the diseases and no exact date, the time of onset was defined as 1 January each year.

Other covariates. Sociodemographic factors, all measured at baseline on 31 December 2005 (ie, before the diagnosis of diabetes) were age (continuous), sex (1=male, 2=female), education (1=compulsory school, 2=high school, 3=university), family situation (1=cohabiting without children, 2=cohabiting with children, 3=living alone, 4=single with children), place of birth (1=born in Sweden, 2=not born in Sweden), and type of living area (1=large city, 2=medium-sized municipality, 3=small municipality).

Statistical analysis

The absolute risk for disability pension was calculated for those with and without diabetes, presented as incidence rates per 1000 person-years. The relative risks were calculated for those with diabetes and compared to the risks of those without diabetes and presented as hazard ratios (HR) with 95% confidence intervals (95% CI), using competing risks models. A competing risks model is a variant of the Cox proportional hazard model. It is based on the fact that – when at risk of disability pension due to a specific diagnosis – individuals are simultaneously at risk of disability pension due to other causes and death, and these risks are mutually exclusive. We included comorbid conditions as time-dependent covariates in the models, which is considered a more robust method of adjusting for confounding, because it utilizes all available data (21).

The individuals were followed from 1 January 2007 through 31 December 2010 or the year they emigrated, until date of death, or date of disability pension, whichever came first. Disability pensioning (=1) and death (=2) were viewed as strongly dependent on health status

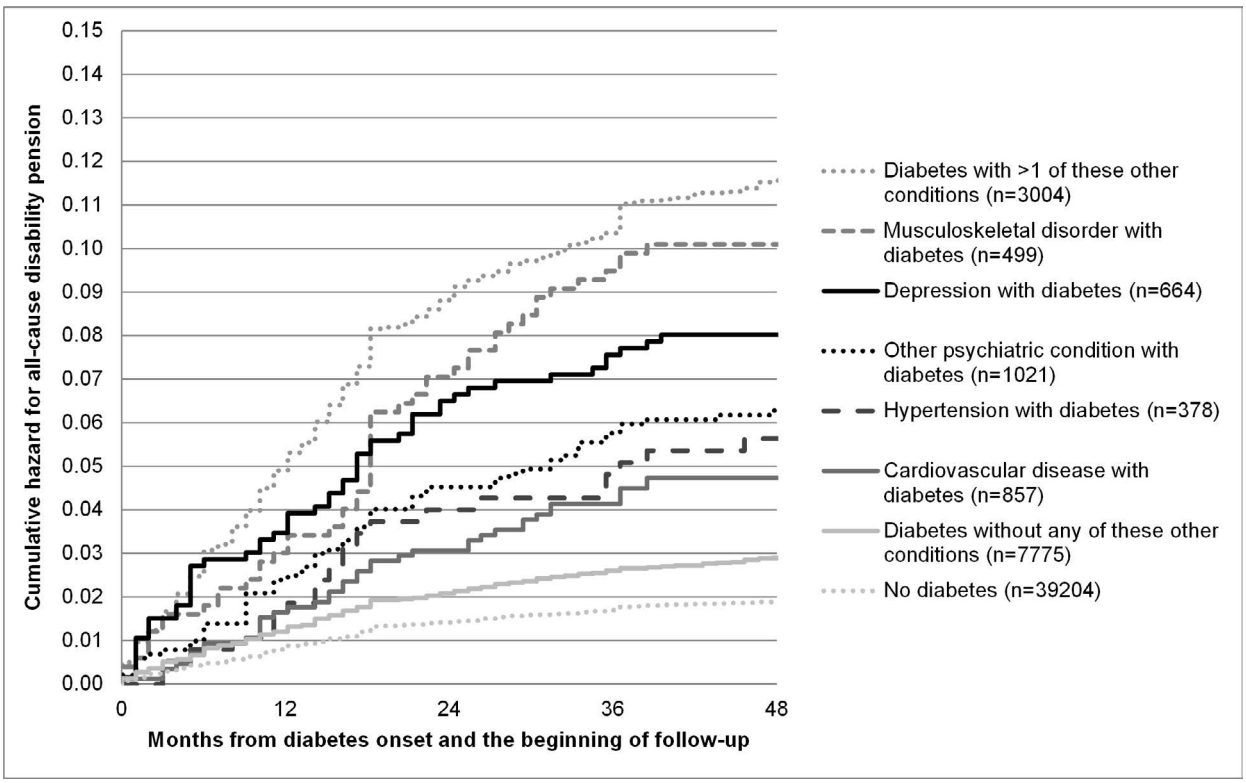

Figure 1. Cumulative probability of all-cause disability pension from the beginning of follow-up for people with and without diabetes (unadjusted) stratified by baseline prevalent other conditions.

Table 1. Sociodemographic characteristics and onset of comorbid conditions among individuals with and without diabetes.

	Diabetes [a]		No diabetes [a]		All [a]	
	N	%	N	%	N	%
Men	8262	58	19 812	51	28 074	53
Women	5936	42	19 392	49	25 328	47
Education						
Low	3713	26	5720	15	9433	18
Intermediate	7159	51	18 989	49	26 148	49
High	3171	23	14 269	36	17 440	33
Type of living area						
Large city	5164	36	14 974	38	20 138	38
Medium-sized city	4856	34	13 777	35	18 633	35
Small city /village	4178	30	10 453	27	14 631	27
Living arrangement						
With a partner, no children	2913	21	4785	12	7698	14
With a partner and children	4914	35	17 440	44	22 354	42
Single, no children	5206	37	13 691	35	18 897	35
Single with children	1165	8	3288	8	4453	8
Born in Sweden	10 539	74	33 507	85	44 046	82
Born in country other than Sweden	3659	26	5697	15	9356	18
Depression 2007–2010	3607	25	5915	15	9522	18
Prevalent in 2007 [b]	2523	70	3653	62	6176	65
Incident during 2008-2010	1084	30	2262	38	3346	35
Other mental disorder 2007–2010	4794	34	7877	20	12671	24
Prevalent in 2007 [b]	3127	65	4234	54	7361	58
Incident during 2008-2010	1667	35	3643	46	5310	42
Cardiovascular disease 2007–2010	3937	28	5481	14	9418	18
Prevalent in 2007 [b]	2251	57	2782	51	5033	53
Incident during 2008-2010	1686	43	2699	49	4385	47
Hypertension 2007–2010	3183	22	1251	3	4434	8
Prevalent in 2007 [b]	1276	40	367	29	1643	37
Incident during 2008–2010	1907	60	884	71	2791	63
Musculoskeletal disorder 2007–2010	3221	23	5811	15	9032	17
Prevalent in 2007 [b]	1182	37	1876	32	3058	34
Incident during 2008-2010	2039	63	3935	68	5974	66

[a] Mean age (SD): diabetes 48.5 (8.8) years; no diabetes 42.0 (9.9) years; all 43.8 (10.0) years.

[b] Illness already at beginning of follow-up.

Table 2. Four-year onset and incidence rate (IR) per 1000 person-years for all-cause disability pension.

Diabetes and comorbidity status	Baseline	Cases ending up on disability pension		
	N	N	%	IR [a]
No diabetes	39 204	898	2.3	5.8
Diabetes without any of these other conditions	7775	290	3.7	9.5
Depression with diabetes	664	62	9.3	23.6
Other psychiatric condition with diabetes	1021	76	7.4	19.9
CVD with diabetes	857	50	5.8	15.0
Hypertension with diabetes	378	29	7.7	19.8
Musculoskeletal disorder with diabetes	499	60	12.0	30.6
Diabetes with >1 of these other conditions	3004	411	13.7	36.5

[a] Incidence rate per 1000 person years: (number of disability pension cases during 4-year follow-up/4 years/number of people at risk)×1000. Those who died during the follow-up are subtracted from people at risk.

(ie, competing events). Emigration was viewed as independent of disability pension or death. Thus, those who emigrated were censored (=0). Regarding diagnosis-specific disability pension, death and receiving disability pension based on diagnosis other than that used as the outcome were defined as competing events (=2).

With regard to Kaplan-Meier curve presented in figure 1, we tested the proportional hazards assumption by including an interaction of each predictor with the log of follow up time. These interactions with time were all nonsignificant, confirming that the proportional hazards assumption was justified (P>0.09). SAS statistical software, version 9.4, was used for all analyses (SAS Institute, Cary, NC, USA).

The contribution of sociodemographic factors and other chronic conditions was determined by the percentage reduction in the coefficient for diabetes status after the inclusion of the covariate in question, using the formula: $100 \times (B_{Model\ 1} - B_{Model\ 2}) / (B_{Model\ 1})$, where Model 1 is the crude and Model 2 the adjusted model.

Results

Those with diabetes were more often men, had a lower level of education, did not have children <18 years of age living in the household, were born outside Sweden, and were somewhat older than those without diabetes. Differences in type of living area were small. Depression, other mental disorders, cardiovascular disease, hypertension, and musculoskeletal disorders were more prevalent among those with diabetes than those without at the beginning of the follow-up (table 1).

Disability pension with and without diabetes

Table 2 shows that the four-year onset and incidence estimates of disability pension were higher among those with diabetes than those without. The incidence of all-cause disability pension was 9.5 per 1000 person-years for those with diabetes only and 5.8 for those without diabetes. The incidence rates varied with comorbid conditions ranging from 15.0 among those with diabetes and cardiovascular disease to 30.6 among those with diabetes and musculoskeletal disorder. Those with diabetes and more than one comorbid condition had the highest incidence of all-cause disability pension, 36.5 per 1000 person-years. Figure 1 shows the hazard curves of time from onset of diabetes until disability pension per comorbid musculoskeletal disorder, depression, other psychiatric condition, cardiovascular disease, and hypertension with diabetes, and also for those without diabetes. Because the event was defined as disability pension, longer survival time indicated a more favor-

Table 3. Contribution of diabetes and incident comorbid conditions to the risk of all-cause disability pension. [CVD=cardiovascular disease.]

	Model 1 [a]		Model 2 [b]		Model 3 [c]		% Attenuation [d]
	HR	95% CI	HR	95% CI	HR	95% CI	
Diabetes [e]	3.11	2.84–3.40	2.30	2.09–2.54	1.63	1.47–1.80	
Depression [e]	.		.		2.93	2.63–3.27	
Other mental [e]	.		.		2.04	1.83–2.28	
CVD [e]	.		.		1.35	1.21–1.50	
Hypertension [e]	.		.		1.50	1.31–1.71	
Musculoskeletal [e]	.		.		1.73	1.54–1.93	
Model 2 versus 1							26
Model 3 versus 1							57
Model 3 versus 2							41

[a] Unadjusted.
[b] Adjusted for sex, age, education, type of living area, family situation, and birth country.
[c] Adjusted as Model 2 and additionally for other conditions.
[d] Attenuation percentage (Model 2 versus 1): $100 \times (B_{Model\ 1} - B_{Model\ 2}) / (B_{Model\ 1})$.
[e] Reference=no.

able outcome. At four-year follow-up, 4% of those with diabetes but without any of the other conditions had ended up on disability pension, whereas for those with comorbid conditions, the percentage ending up on disability pension varied between 6% and 14%, depending on comorbid condition (figure 1). As also shown in figure 1, only 2% of those without diabetes ended up on disability pension.

The mean follow-up time was 46 months (SD 9.5) for those with diabetes and 48 months (SD 5.9) for those without. During the follow-up, 100 (0.7%) of those with diabetes and 433 (1.1%) of those without diabetes emigrated from Sweden. A total of 482 (3.4%) of those with and 307 (0.8%) of those without diabetes died during the follow-up. The crude relative risk for all-cause disability pension was 3.11-fold (95% CI 2.84–3.40, Model 1) for people with diabetes compared to those without. Adjustment for sociodemographic factors attenuated this risk by 26% (HR 2.30, 95% CI 2.09–2.54, Model 2) (table 3).

Contribution of comorbid conditions

Other conditions also contributed to the risk of disability pension: further adjustment for other conditions attenuated the risk of all-cause disability pension by 41% when compared to the sociodemographics-adjusted model (HR 1.63, 95% 1.47, 1.80, Model 3). Specifically, depression (HR 2.93, 95% CI 2.63–3.27) and other mental disorders (HR 2.04, 95% CI 1.83–2.28) constituted a greater risk factor for all-cause disability pension than diabetes.

The results regarding disability pension based on mental disorders, musculoskeletal disorders, and diseases of the circulatory system are shown in supplementary tables B–E (www.sjweh.fi/data_repository.php). The incidence of disability pension due to mental disorders, musculoskeletal disorders and diseases of the circulatory system was at least twice as common among those with diabetes as among those without (4.7 versus 2.1 for mental, 3.6 versus 1.5 for musculoskeletal, and 2.8 versus 0.5 for circulatory diseases) (supplementary table B).

Mental disorders were the strongest predictor of disability pension due to mental disorders (HR 6.81; 95% CI 5.52–8.40 for depression; HR 4.44; 95% CI 3.58–5.49 for other psychiatric disorders); musculoskeletal disorders were the strongest predictor of disability pension due to musculoskeletal disorders (HR 5.34; 95% CI 4.37–6.53); and cardiovascular disease was the strongest predictor of disability pension due to circulatory system disease (HR 7.36, 95% CI 5.32–10.19). Having diabetes was associated with an increased risk of disability pension due to musculoskeletal disorders and circulatory system disease. However, adjustment for mental disorders diluted the effect of diabetes as a risk factor for disability pension due to mental disorders. In the sociodemographics-adjusted model, diabetes was associated with a 2.02-fold (95% CI 1.70–2.41) risk of disability pension due to mental disorders, a 1.59-fold (95% CI 1.32–1.94) risk of disability pension due to musculoskeletal disorders, and a 5.99-fold (95% CI 4.25–8.44) risk of disability pension due to cardiovascular diseases. Adjustment for other conditions attenuated the risk of disability pension due to musculoskeletal disorders by 65% when compared to the sociodemographics-adjusted model. The corresponding decrease in disability pensions due to circulatory system disease was 48%. In the fully-adjusted models, diabetes was associated with a 1.17-fold (95% CI 0.98–1.40) risk of disability pension due to mental disorders, a 1.37-fold (95% CI 1.12–1.67) risk of disability pension due to musculoskeletal disorders, and a 3.30-fold (95% CI 2.30–4.72) risk of disability pension due to diseases of the circulatory system.

Discussion

This nation-wide prospective study among the population of Sweden showed that people with diabetes were, in both relative and absolute terms, at a higher risk of all-cause disability pension than those without diabetes during a four-year follow-up. The established socio-demographic risk factors for disability pension (20, 22), such as older age, female sex, and lower educational level, explained 26% of this excess risk. Moreover, adjusting for comorbid conditions further attenuated the risk by 41%.

In relative terms, depression and other mental disorders constituted a greater risk factor for all-cause disability pension than diabetes. In diagnosis-specific analyses, we found that diabetes was a risk factor for disability pension due to musculoskeletal disorders and diseases of the circulatory system, even after accounting for the above-mentioned conditions. However, diabetes was not a risk factor for disability pension due to mental disorders after accounting for comorbid other conditions. This indicates that diabetes has an independent effect on the risk of disability pension, and especially on the risk disability pension due to musculoskeletal disorder or circulatory system disease. However, comorbid mental disorder contribute to that risk to a large degree. Earlier studies have found that diabetes was associated with a 37% lower probability of return to work after depression-related absence (23) and a 43% higher probability of recurrent depression-related absence (24). Disability pension due to diseases of the circulatory system among people with diabetes is possibly directly associated with diabetes-related complications, such as coronary heart disease or stroke (17, 25). Diabetes-related complications also include disorders of the musculoskeletal system, such as Dupuytren's contracture, carpal tunnel syndrome, neuropathic osteoartropathy, and osteoarthritis (18, 26), which may even lead to permanent work disability, ie, disability pension. Finally, pre-existing conditions including diabetes explained why older age was associated with longer sickness absence following musculoskeletal injury (27).

The results corroborate earlier evidence regarding the effect of diabetes and comorbid conditions on the excess risk of work disability (6-8). The study contributes to existing evidence by using comorbid conditions as time-dependent covariates and treating other diagnoses of disability pension as competing events (in diagnosis-specific analyses). In doing this, we were better able to demonstrate and isolate the direct effect of diabetes on all-cause and diagnosis-specific disability pension.

In addition to sophisticated methods of analysis, this study benefits from the large population-based prospective cohort study design and reliable register-based measures with high coverage and specificity (28). Though the validity of disability pension diagnoses was not studied, sick leave diagnosis showed a high validity compared to diagnoses from medical records (29). We also had a longer follow-up time than that reported in previous studies on the role of diabetes and comorbid conditions in work disability (6, 7).

Limitations

The limitations include the fact that we did not reach cases of undiagnosed diabetes or those treated by lifestyle intervention only. We may also have missed some individuals with diabetes in 2003–2005 since data on medication purchases was from July 2005 only. However, in Sweden, you can only buy a maximum of three months' supply of medication at a time. Thus, as most people diagnosed with diabetes should have bought medication at least once during July–December, 2005, this purchase would have coded them as having diabetes in 2003–2005 and resulted in their exclusion from the data. The in- and out-patient records for 2003–2005 were from specialized healthcare, and part of diabetes care is carried out in primary healthcare. However, most of the cases managed in primary healthcare should have been identified through medication purchases. We were unable to identify some common complications of diabetes, such as neuropathy and retinopathy. Finally, people with chronic conditions such as diabetes, cardiovascular disease, or hypertension use more healthcare services and are thus more likely to be diagnosed with other conditions as well. This may lead to the overrepresentation of comorbid conditions among people with diabetes and the subsequent overestimation of the role of comorbidity in the association between diabetes and disability pension.

When interpreting these findings, we must acknowledge that, in some cases, diabetes may have caused the comorbid condition. In some cases, both may be a consequence of a common underlying factor. And in other cases, diabetes and the comorbid conditions may be causally unrelated. In all-cause disability pensions, it is possible that disability pension was granted due to diseases other than those we studied, causing unmeasured residual confounding. Thus, we are not able to make causal conclusions on the basis of the current study. Finally, our data lacked information on diabetes severity or diabetes control. However, the fact that the onset of diabetes occurred during the same year for all participants with diabetes somewhat dilutes the effect of the lack of this information.

Concluding remarks

In conclusion, although having diabetes is a risk factor for disability pension, comorbid conditions greatly

contribute to this excess risk. Moreover, diabetes as a comorbid condition to mental and musculoskeletal disorders or diseases of the circulatory system constituted a risk factor for disability pension. Thus, comprehensive health examinations and especially the treatment of the mental health of people with diabetes may prevent permanent loss of working capacity.

Conflict of interest and sources of funding

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