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Accumulated exposure to unemployment is related to impaired glucose metabolism in middle-aged men: A follow-up of the Northern Finland Birth Cohort 1966



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ABSTRACT

Aims: We explored whether registered unemployment is associated with impaired glucose metabolism in general population.

Methods: Based on Northern Finland Birth Cohort 1966 at 46 years, we analyzed the oral glucose tolerance tests of 1970 men and 2544 women in relation to their preceding three-year employment records in three categories of unemployment exposure: no (employed), low (≤ 1 -year) and high exposure (> 1 -year).

Results: Among men, pre-diabetes was found in 19.2% of those with no unemployment, 23.0% with low and 27.0% with high exposure, the corresponding figures for screen-detected type 2 diabetes were 3.8%, 3.8% and 9.2% ($p < 0.01$). Among women, analogous figures for pre-diabetes were 10.0%, 12.6% and 16.2% and for screen-detected type 2 diabetes 1.7%, 3.4%

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and 3.6% ($p < 0.01$). Men with high exposure to unemployment had a higher risk for pre-diabetes (OR 1.61, CI 95% 1.03–2.51) and screen-detected type 2 diabetes (OR 2.58 95% CI 1.23–5.44) than employed men, after adjustment for education, smoking, alcohol intake, physical activity and body mass index. Among women, associations were attenuated in the adjusted models.

Conclusions: High exposure to unemployment may predispose to type 2 diabetes in middle-aged men. For clinicians, awareness of the patient's unemployment status may be helpful in recognizing undiagnosed cases.

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1. Introduction

Type 2 diabetes is a growing global epidemic with a large adverse economic impact [1]. Etiologically, the current knowledge posits a complex interplay between biological, psychological and social factors during the life-course [2–4]. The disease develops through a long-term process characterized by asymptomatic pre-diabetic states with heightened glycaemia [2]. Intervention studies have however shown, that the progression towards type 2 diabetes can be prevented or delayed by lifestyle interventions in high-risk individuals [5,6]. In a 45–74 year-old general population sample, high prevalences were found for asymptomatic pre-diabetes (26% of men and 22% of women) and test-detected type 2 diabetes (9% of men and 7% of women) in oral glucose tolerance tests (OGTT) [7]. Therefore, feasible practices are needed for clinicians to recognize high risk individuals for timely diagnostics and treatment.

Prolonged stress is suggested to be causally linked to the onset of type 2 diabetes [8–10] through overactivity of the hypothalamo–pituitary–adrenal (HPA) axis and cortisol production, as well as behavioral factors [11]. Type 2 diabetes typically occurs in the working age with incidence peaking between 40–64 years [12]. It is hypothesized that employment-related stressors could underlie the development of type 2 diabetes. Stressors such as job strain [13–15] and shift work [13,16] have been shown to predict type 2 diabetes independently of health behaviors [13,15,16]. Some of these results have shown gender-specificity. For instance, work-related stress and shift work have increased the risk of type 2 diabetes in women, whereas high demands and high strain have reduced this risk in men [13,15]. In a large pooled analysis however, job strain increased the risk for type 2 diabetes irrespective of gender [14]. Whilst there are biological and social backgrounds to support sex-specific variations in the etiology of type 2 diabetes in relation to employment patterns, more analysis in both men and women is needed to explore the association between working life and type 2 diabetes.

Unemployment is a common stressor in the working life [17] and a known risk factor for poor health [18]. Nevertheless, only few studies have studied its relation to the development of diabetes, and only based on self-reported unemployment [19–21]. One of these linked type 2 diabetes to individually reported unemployment in women, and to neighbourhood-level aggregates in men [19]. Recently, a systematic review on

the effects of employment on health concluded that although employment appears generally beneficial for health, in particular mental health, further research is needed in relation to specific physical effects of public health relevance [22]. Diabetes is one of the most relevant public health concerns warranting further study in relation to working life.

The present study, based on of the Northern Finland Birth Cohort 1966 (NFBC1966), explores the relation between varying lengths of unemployment with the risk of pre-diabetes and type 2 diabetes in the general population. To our best knowledge, this is the first study to test for the association with objective data for both the exposure to unemployment (national registers) and the outcome of glucose metabolism (OGTT) in men and women.

2. Methods

This study is part of the NFBC 1966 study, based on 12,058 live-born children, whose expected dates of birth were in 1966 (96.3% of all births in the region) in the provinces of Oulu and Lapland (Fig. 1) [23]. The prospective data comprises data from questionnaires, clinical examinations and national registers.

The latest 46-year follow-up was conducted between April 2012 and February 2014. The target population consisted of 10,331 eligible individuals, who were alive and living in Finland (84.5% of the original birth cohort, Fig. 1), whereof 65.3% completed the questionnaire concerning education and lifestyle factors. In the clinical examination, 4925 individuals without previously diagnosed diabetes and consenting to the study participated in the OGTT (Fig. 1).

2.1. Glucose metabolism

Previous diabetes was defined according to self-reported diagnoses and medications, hospital registers and medication registers from Social Insurance Institution of Finland. For those without previous diabetes, OGTT was conducted in the morning after an overnight fast with 0, 0.5, 1 and 2-h blood samples with glucose determinations from plasma (mmol/L) (Advia 1800, Siemens Healthcare Diagnostics Inc., Tarrytown, Ny, USA Country). Before the OGTT, capillary fingertip blood glucose was measured (Ascensia Contour, Bayer Inc., Canada) and if greater than 8.0 mmol/L, only a fasting glucose sample was taken ($n = 28$). For others, the OGTT was performed by standardized protocol i.e. ingestion of a bolus providing 75 g

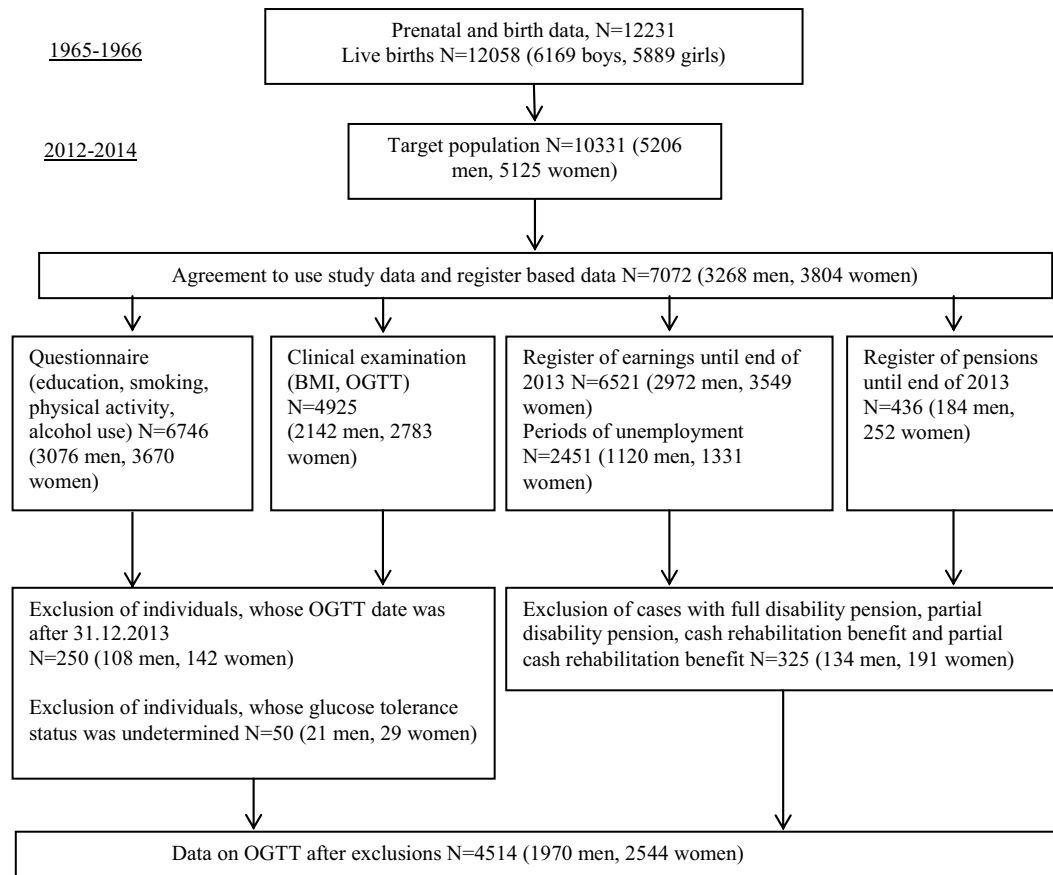


Fig. 1 – Flow-chart of the study population in the NFBC 1966.

glucose (GlucosePro, Comed, Finland) within five minutes after the baseline blood sample. All participants received their fasting glucose or OGTT results by mail to be communicated with their local primary health care centers.

The glucose tolerance status was classified according to WHO 1999 criteria [24]: impaired fasting glucose (IFG): fasting glucose ≥ 6.1 mmol/L but < 7.0 mmol/L and 2-h glucose < 7.8 mmol/L, impaired glucose tolerance (IGT): 2-h plasma glucose concentration ≥ 7.8 and < 11.1 mmol/L and fasting plasma glucose < 7.0 mmol/L and screen-detected type 2 diabetes: fasting glucose ≥ 7.0 mmol/L and/or 2-h glucose ≥ 11.1 mmol/L. Individuals with IFG or IGT were combined and categorized as having pre-diabetes.

2.2. Unemployment

Data on all earning periods (as an employee or an entrepreneur), unpaid periods and pension periods were obtained from the Finnish Centre for Pensions (FCP) during the individually determined three-year periods preceding the day of the OGTT. The individual numbers of unemployment days were extracted from the following unpaid periods: the periods when the individual received basic or earnings-based unemployment allowance, daily allowance for entrepreneur, labor market subsidy, employment services' training support, or unemployment training allowance. In order to receive any of these allowances, the individual had to confirm his/her

unemployment days for the employment agency either electronically or by signature on a regular basis (every four weeks). Because unemployment allowance is paid for 5 days per week and 52 weeks per year (261 days/year), the potential exposure to unemployment ranged from 0 to 784 days during the three-year period including one leap year. We classified the levels of exposure to the unemployment days as follows: 0 days if earning periods covered the whole follow-up (=no unemployment), 1–261 days representing amount of one calendar year or less (=low exposure to unemployment), and 262–784 days representing more than one calendar year during the three-year follow-up (=high exposure to unemployment).

2.3. Inclusion criteria

In order to only include active individuals belonging to the work force with a true potential for exposure to unemployment, we excluded the individuals on disability benefits during the three-year period: those who started a full or partial permanent disability pension or a cash rehabilitation benefit indicating a fixed-term disability pension (Fig. 1). Since these benefits are granted after medically certified sickness absence has lasted one year [25], the individuals on their way to exiting the work force due to disabilities were excluded. Shorter sickness absences that get paid by the employer, with differing amounts in differing work contracts, are by definition not unpaid periods and thus not extractable from the earn-

ing periods. Shorter sickness absences do not contradict the belonging to the work force. Also those individuals with short unpaid periods compensated by rehabilitation allowance were included in the study since this allowance requires an ongoing work contract and is only granted if there is a high potential for continuing working.

With the register data coverage until 31.12.2013, those 250 individuals clinically examined in 2014 had incomplete employment records preceding the day of OGTT and had to be excluded from the study. In addition, 50 individuals with incomplete OGTT results were excluded. The final sample consisted of 1970 men and 2544 women with complete data on OGTT (Fig. 1).

2.4. Covariates

We used the level of education to measure the socioeconomic status. Based on two survey questions on basic and vocational education, the educational level was classified as basic (≤ 9 years of school and no vocational education or only short course), secondary (vocational school or college degree and/or matriculation examination) or tertiary (polytechnic or university degree).

Lifestyle factors surveyed were smoking, alcohol intake and physical activity. Smoking was categorized as current, former and non-smokers. Use of alcohol was measured on the average consumption including the frequency and the amount of each type of beverages (beer, wine and spirits) per drinking occasion and calculated into grams per day (g/day), further classified according to tertiles separately for men and women. Leisure time physical activity was based on a question asking “How much physical activity do you practice during leisure time?” with response categories: (1) I read, watch TV and perform activities which do not physically strain me, (2) I walk, ride a bicycle or otherwise practice exercise at least 4 h per week, (3) I practice physical activity to maintain physical condition such as running, jogging, cross-country skiing, swimming at least 2 h per week and (4) I practice regularly for competition such as running, orienteering, cross-country skiing, swimming and ball games. Class 1 was defined as low, class 2 as moderate and classes 3–4 as high physical activity.

Weight (kg) and height (cm) were measured from participants in underwear and barefoot. Body mass index (BMI) was calculated as weight (kg) divided by the squared height (m^2).

2.5. Ethical statement

The study was approved by the Ethics Committee of the Northern Ostrobothnia Hospital District. All participants gave written informed consent.

2.6. Statistical analyses

The analysis was conducted separately for men and women using SAS 9.4. (SAS Institute Inc., Cary, NC, USA). Cross-tabulation, χ^2 -test, t-test and analysis of variance (ANOVA) were used to test differences between the exposure to unemployment and education, smoking, alcohol intake, physical activity, BMI and glucose metabolism. Population attributable risk (PAR) indicating the proportion of cases of screen-detected

pre-diabetes and type 2 diabetes that would not occur without high exposure to unemployment was also calculated. Finally, multinomial logistic regression analyses were used to test the risk for pre-diabetes and screen-detected type 2 diabetes (normal glucose tolerance was set as a reference group) at follow-up according to exposure of unemployment. Four models were tested, unadjusted (model 1), adjusted for education only (model 2), adjusted for smoking, alcohol, physical activity and BMI (model 3) and adjusted for all covariates (model 4). Gender differences in associations between unemployment and glucose metabolism were tested with an interaction test for unemployment and gender.

3. Results

3.1. Population characteristics

During the three-year follow-up, more than a fifth of the men and women had been exposed to unemployment (Table 1). In comparison to those employed, the individuals exposed to unemployment, irrespective of gender and amount of joblessness, were more often less educated, smokers and less physically active. Furthermore, women with high exposure to unemployment had a higher BMI than employed women (Table 1).

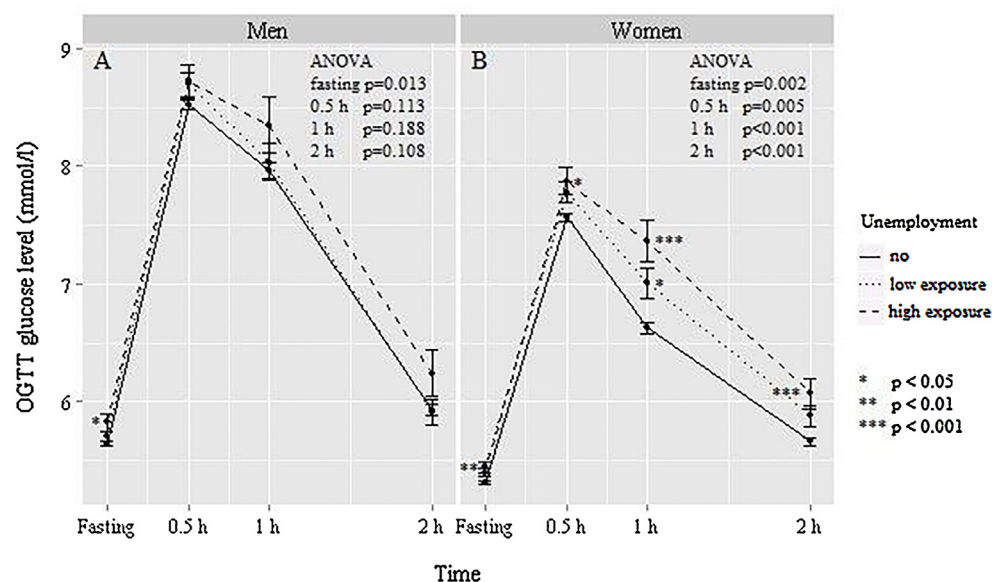
3.2. Glucose metabolism and exposure to unemployment

The mean glucose response to OGTT at follow-up in each unemployment category is shown in Fig. 2. Irrespective of the unemployment history, men had much higher glucose concentrations than women at all measurement points of the OGTT ($p < 0.001$ in all models). Men with high exposure to unemployment had 3.2% higher fasting glucose than employed men, whereas the glucose concentrations at times 0.5 h, 1 h and 2 h did not significantly differ by the employment groups due to larger differences in standard deviations. Compared to the employed women, women with low exposure to unemployment had 2.4% higher fasting and 5.7% higher 1-h glucose concentrations. The OGTT results of the women with high exposure to unemployment significantly differed from those employed, with 4.1%, 11.2% and 7.2% higher 0.5 h, 1-h and 2-h mean glucose concentrations, respectively.

Overall, we detected 686 individuals with pre-diabetes, 403 (20.5%) men and 283 (11.1%) women. In addition, 136 individuals were OGTT-screened as type 2 diabetic, 83 (4.2%) men and 53 (2.1%) women ($p < 0.001$ for gender difference). The prevalence of screen-detected pre-diabetes and type 2 diabetes rose in an almost stepwise manner in relation to the categories of exposure to unemployment in men ($p = 0.001$) and to a lesser extent in women ($p = 0.006$) (Table 2). Among men with high unemployment exposure, 4.1% of the risk of pre-diabetes could be attributed to unemployment, and the corresponding figure for women was 6.0%. Strikingly, among men with high exposure to unemployment, 13.1% of the risk of screen-detected type 2 diabetes was attributable to unemployment, and the corresponding attributable risk was 10.3% for the women with high exposure to unemployment.

Table 1 – Characteristics of men and women at the age of 46 years according to unemployment days during the three-year period before entering oral glucose tolerance test.

	Unemployment													
	Men							Women						
	0 days		≤1y		≥1y			0 days		≤1y		≥1y		
	n	%	n	%	n	%	p-Value	n	%	n	%	n	%	p-Value
	1295	76.8	239	14.2	152	9.0		1733	78.8	269	12.2	197	9.0	
Education														
Basic	75	6.1	18	7.8	28	19.6	<0.001	54	3.2	19	7.2	28	14.7	<0.001
Secondary	823	66.4	176	75.9	90	62.9		1074	63.5	181	68.3	123	64.7	
Tertiary	341	27.5	38	16.4	25	17.5		563	33.3	65	24.5	39	20.5	
Smoking														
Current smoker	207	16.9	44	19.2	51	35.7	<0.001	243	14.5	44	16.9	50	26.6	0.0008
Former smoker	368	30.0	81	35.4	35	24.5		426	25.4	63	24.2	42	22.3	
Non-smoker	653	53.2	104	45.4	57	39.9		1011	60.2	153	58.9	96	51.1	
Alcohol intake ^a														
0–4 g/0–1.3 g/day	413	33.3	62	26.7	55	38.5	0.052	554	32.7	95	35.9	68	35.8	0.519
4.1–15.2 g/1.4–5.9 g/day	425	34.3	85	36.6	36	25.2		575	34.0	95	35.9	61	32.1	
>15.2 g/>5.9 g/day	401	32.4	85	36.6	52	36.4		563	33.3	75	28.3	61	32.1	
Physical activity														
Low	229	18.6	39	17.0	35	24.7		300	17.8	56	21.2	51	27.1	
Moderate	454	36.9	119	52.0	70	49.3		649	38.4	123	46.6	96	51.1	
High	546	44.4	71	31.0	37	26.1	<0.001	740	43.8	85	32.2	41	21.8	<0.001
BMI, mean (SD) ^b	1292	27.2 (4.0)	238	27.1 (4.1)	151	27.1 (4.5)	0.922	1728	26.0 (4.8)	269	26.1 (5.0)	197	27.3 (5.4)**	0.002

* $p \leq 0.05$.** $p \leq 0.01$.*** $p \leq 0.001$.^a Tertiles calculated separately for men and women.^b Employed group was defined as a reference group in pairwise comparisons.**Fig. 2 – Fasting glucose, 0.5-h-, 1-h and 2-h glucose (mmol/L) in men and in women at the 46-year follow-up in the NFBC 1966 (means and standard errors).**

As Table 2 shows, the observed 1.6-fold odds for pre-diabetes and 2.6-fold odds for screen-detected type 2 diabetes for men with high exposure to unemployment compared to employed men remained statistically significant even after

adjustment for education, lifestyle factors and BMI. Among women with high exposure to unemployment, the corresponding associations were visible in the unadjusted model, but attenuated after adjustments for lifestyle factors and BMI.

Table 2 – Prevalence and multinomial logistic regression analyses for pre-diabetes and type 2 diabetes (normal glucose tolerance as a reference category) according to unemployment during the three-year period before entering the oral glucose tolerance test in middle aged men and women.

		N	%	OR (95% CI) Model 1	OR (95% CI) Model 2 ^a	OR (95% CI) Model 3 ^b	OR (95% CI) Model 4 ^c
Prediabetes							
Unemployment							
Men	0	249	19.2	1.0	1.0	1.0	1.0
	≤1y	55	23.0	1.26 (0.90–1.76)	1.26 (0.90–1.78)	1.28 (0.89–1.85)	1.26 (0.88–1.82)
	>1y	41	27.0	1.69 (1.15–2.50)	1.59 (1.06–2.39)	1.60 (1.03–2.49)	1.61 (1.03–2.51)
Women	0	173	10.0	1.0	1.0	1.0	1.0
	≤1y	34	12.6	1.33 (0.90–1.97)	1.30 (0.87–1.95)	1.30 (0.86–1.96)	1.30 (0.85–1.97)
	>1	32	16.2	1.79 (1.19–2.70)	1.69 (1.10–2.61)	1.32 (0.83–2.08)	1.37 (0.86–2.17)
Type 2 diabetes							
Unemployment							
Men	0	49	3.8	1.0	1.0	1.0	1.0
	≤1y	9	3.8	1.05 (0.51–2.17)	1.03 (0.50–2.14)	1.14 (0.52–2.51)	1.12 (0.51–2.47)
	>1y	14	9.2	2.94 (1.57–5.52)	2.64 (1.34–5.19)	2.43 (1.17–5.07)	2.58 (1.23–5.44)
Women	0	29	1.7	1.0	1.0	1.0	1.0
	≤1y	9	3.4	2.10 (0.98–4.50)	2.04 (0.95–4.39)	2.05 (0.89–4.69)	2.02 (0.88–4.64)
	>1y	7	3.6	2.34 (1.01–5.43)	2.18 (0.92–5.18)	1.89 (0.78–4.60)	1.80 (0.72–4.49)

^a Adjusted for education.^b Adjusted for smoking, alcohol intake, physical activity and BMI.^c Adjusted for education, smoking, alcohol intake, physical activity and BMI.

In the unadjusted model including both genders (data not shown), the interaction term for unemployment and gender was nonsignificant ($p = 0.692$).

4. Discussion

In this middle-aged general population cohort, as much as a fifth of men and a tenth of women were found to have previously undiagnosed pre-diabetes or type 2 diabetes. The prevalence of the impaired glucose metabolism rose in a stepwise manner according to the categories of preceding exposure to unemployment in both men and women. Among individuals with high exposure to unemployment (over a year) and screen-detected type 2 diabetes, 13.1% of the diabetes risk was attributable to unemployment in men and 10.3% in women. Compared to those employed, men with high exposure to unemployment had a 1.6-fold risk for pre-diabetes and 2.6-fold risk for screen-detected type 2 diabetes after adjustment for education, lifestyle factors and BMI. Among women the analogous association was attenuated after adjustment for lifestyle factors and BMI.

Previous literature suggests a bi-directional association between unemployment and health, i.e. individuals with poor health tend to drift towards unemployment and unemployment tends to lead to deteriorating health [26]. The underlying potential pathways include prolonged stress resulting from economic hardship, loss of self-esteem and loss of the health promoting aspects available at the workplace [18,27] further leading to chronic alteration of the stress response within the HPA axis and/or through deteriorating health behavior [11]. Stress has indeed been previously found to predict pre-diabetes [9] and type 2 diabetes [9,10] beyond the traditional behavioural risks.

In this study, adjustments for education, lifestyle factors and BMI produced differing results in men and women. We found a robust association between high exposure to unemployment and impaired glucose metabolism in men, independent from education, lifestyle factors and BMI, while in women the corresponding observed risk for pre-diabetes and screen-detected type 2 diabetes in the unadjusted model was explained by lifestyle factors and BMI. Although a moderation effect of gender was not supported by an interaction test, our results accord with one previous study reporting that the association between self-reported unemployment and type 2 diabetes could be explained by physical activity and BMI in women [19]. We note that in our sample the men were overall in worse glycemic health than the women. In their late 40s, most of the women were still in a premenopausal stage which has been consistently reported to protect or delay the onset of disorders in glucose metabolism [28]. Additional research focusing on gender differences remains needed.

The strength of this study is the objective register-based quantification of exposure to unemployment during a precise three-year follow-up period preceding an OGTT, capturing the important acute exposure to unemployment-related hardships during the early stages of diabetogenesis. Since the participants are of the same age, the analysis is not biased by temporal macroeconomic fluctuations in general unemployment rates, which may affect the health effects of unemployment [29]. Adding to the studies conducted within occupational cohorts, our general population approach covers all branches of economy and provides insight to working life issues of both genders. A likewise important strength arises from the objective outcome measure of the OGTT, not restricted to fasting state but harnessing the dynamics of glucose metabolism. The main limitation of the study is the lack of baseline assessment of glucose metabolism prior to the

exposure of unemployment that might have allowed us to further address the question of causality. We were not either able to adjust for medications influencing glucose levels, for example corticosteroids. If there had occurred selection of diabetic individuals towards unemployment during the three-year follow-up period, our figures concerning the association of unemployment and diabetes could be overestimated. It is also possible, that unemployed participants with poor health may have dropped out before the 46-year follow-up study more often than the employed individuals, leading to an underestimation of the association. In an observational study, residual confounding always remains a possibility.

We emphasize, that all the screen-detected type 2 diabetes and pre-diabetes cases found in this large general population sample had been undiagnosed before the OGTT. Therefore, our results can be interpreted in terms of the notable screening potential of unemployment history, to detect undiagnosed impaired glucose metabolism in the encounters of health care. In addition, knowledge on the higher risk for type 2 diabetes in unemployed individuals could be helpful for the unemployed individuals themselves. It is estimated that each year, 5–10% of individuals with pre-diabetes will develop type 2 diabetes and that the same proportion will convert back to normoglycaemia [30], with lifestyle modifications as the cornerstone of diabetes prevention. It is crucial to target preventive actions to the individuals at highest risk for type 2 diabetes at the earliest possible time point.

5. Conclusions

To the best of our knowledge, this is the first study to objectively quantify the relation between varying exposure to unemployment and impaired glucose metabolism. Our results suggest an independent relation of unemployment and type 2 diabetes in men. In clinical practice, the readily available anamnestic information on recent unemployment might be helpful in recognizing high risk and considering screening for diabetes in middle-aged individuals.

Conflict of interest

The authors state that they have no conflict of interest.

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