International Journal of Public Health

The association of unemployment with glucose metabolism: a systematic review and meta-analysis

--Manuscript Draft--

Manuscript Number: IJPH-D-17-00406R3

Full Title: The association of unemployment with glucose metabolism: a systematic review and meta-analysis

Article Type: Review

Keywords: unemployment; glucose metabolism; prediabetes; type 2 diabetes; systematic review; meta-analysis

Corresponding Author: Tuulia Varanka-Ruuska, M.D.

University of Oulu, Oulu, Finland

Oulu, FINLAND

Corresponding Author Secondary

Information:

Corresponding Author's Institution: University of Oulu, Oulu, Finland

Corresponding Author's Secondary

Institution:

First Author: Tuulia Varanka-Ruuska, M.D.

First Author Secondary Information:

Order of Authors: Tuulia Varanka-Ruuska, M.D.

Nina Rautio, Ph.D

Heli Lehtiniemi, M.Sc.

Jouko Miettunen, Ph.D.,Professor

Sirkka Keinänen-Kiukaanniemi, M.D., Ph.D.,Professor

Sylvain Sebert, Ph.D.,Adjunct Professor

Leena Ala-Mursula, M.D., Ph.D.,Professor

Order of Authors Secondary Information:

Manuscript Region of Origin: FINLAND

Funding Information: Academy of Finland

(#268336)

Mr. Jouko Miettunen

Horizon 2020

(633595)

Mr. Sylvain Sebert

Horizon 2020

(No 633595)

Ms. Nina Rautio

Abstract: Objectives: Unemployment has been linked with poor health. We hypothesized that being unemployed is associated with disorders of glucose metabolism and performed a systematic review and meta-analysis of the literature to ascertain the relationship.

Methods: We searched the databases of Scopus, Medline Ovid and Web of Science for population-based original studies for past 20 years. Random effects meta-analyses were used to estimate odds ratios (OR) with 95% confidence intervals (CI) for prediabetes and type 2 diabetes among the unemployed as compared to those employed, separately for men and women when possible.

Results: Out of 981 articles found, 12 articles were included in the systematic review and eight articles in the meta-analyses. Unemployment was associated with 1.6-fold odds for prediabetes (OR 1.58; 95%CI 1.07-2.35), and 1.7-fold odds for type 2 diabetes (OR 1.72; 95%CI 1.14-2.58) in the total sample. The corresponding associations for type 2 diabetes were also found stratified for men (OR 1.53; 95%CI 1.47-1.60) and women (OR 1.60; 95%CI 1.33-1.92).

Conclusions: Unemployment is associated with prediabetes and type 2 diabetes, global concerns of public health with potential for prevention.

The association of unemployment with glucose metabolism: a systematic review and meta-analysis

Tuulia Varanka-Ruuska1,2, Nina Rautio1,3, Heli Lehtiniemi1, Jouko Miettunen1,4, Sirkka Keinänen-Kiukaanniemi1,3,4,5,

Sylvain Sebert1,6,7, Leena Ala-Mursula1

1 Center for Life Course Health Research, P.O. Box 5000, 90014 University of Oulu, Oulu, Finland

2 Kallio Primary Health Care Unit, Kirkkotie 4, 84100 Ylivieska, Finland

3 Unit of Primary Health Care, Oulu University Hospital, P.O. Box 20, 90029 OYS, Oulu, Finland

4 Medical Research Center Oulu, Oulu University Hospital and University of Oulu, P.O. Box 5000, 90014 Oulu, Finland

5 Health Center of Oulu, P.O. Box 27, 90015 Oulu, Finland

6 Biocenter Oulu, University of Oulu, P.O. Box 5000, 90014 Oulu, Finland

7 Department of Genomics of Complex Diseases, Imperial College, London, South Kensington Campus, London SW7

London, United Kingdom

Corresponding author: Tuulia Varanka-Ruuska, Center for Life Course Health Research, P.O. Box 5000, 90014

University of Oulu, Oulu, Finland

Email: tuulia.varanka-ruuska@oulu.fi

Telephone: +358406744525

Fax: +35885375661

Conflict of interest

Author Tuulia Varanka-Ruuska declares she has no conflicts of interest. Author Nina Rautio declares she has no conflicts

of interest. Author Heli Lehtiniemi declares she has no conflicts of interest. Author Jouko Miettunen declares he has no

conflicts of interest. Author Sirkka Keinänen-Kiukaanniemi declares she has no conflicts of interest. Author Sylvain

Sebert declares he has no conflicts of interest. Author Leena Ala-Mursula declares she has no conflicts of interest.

Contact details

Abstract

Objectives: Unemployment has been linked with poor health. We hypothesized that being unemployed is associated with disorders of glucose metabolism and performed a systematic review and meta-analysis of the literature to ascertain the relationship.

Methods: We searched the databases of Scopus, Medline Ovid and Web of Science for population-based original studies for past 20 years. Random effects meta-analyses were used to estimate odds ratios (OR) with 95% confidence intervals (CI) for prediabetes and type 2 diabetes among the unemployed as compared to those employed, separately for men and women when possible.

Results: Out of 981 articles found, 12 articles were included in the systematic review and eight articles in the metaanalyses. Unemployment was associated with 1.6-fold odds for prediabetes (OR 1.58; 95%CI 1.07-2.35), and 1.7-fold odds for type 2 diabetes (OR 1.72; 95%CI 1.14-2.58) in the total sample. The corresponding associations for type 2 diabetes were also found stratified for men (OR 1.53; 95%CI 1.47-1.60) and women (OR 1.60; 95%CI 1.33-1.92).

Conclusions: Unemployment is associated with prediabetes and type 2 diabetes, global concerns of public health with potential for prevention.

The association of unemployment with glucose metabolism: a systematic review and meta-analysis

Tuulia Varanka-Ruuska1,2, Nina Rautio1,3, Heli Lehtiniemi1, Jouko Miettunen1,4, Sirkka Keinänen-Kiukaanniemi1,3,4,5,

Sylvain Sebert1,6,7, Leena Ala-Mursula1

1 Center for Life Course Health Research, Oulu, Finland

2 Kallio Primary Health Care Unit, Ylivieska, Finland

3 Unit of Primary Health Care, Oulu University Hospital, Oulu, Finland

4 Medical Research Center Oulu, Oulu University Hospital and University of Oulu, Oulu, Finland

5 Health Center of Oulu, Oulu, Finland

6 Biocenter Oulu, University of Oulu, Oulu, Finland

7 Department of Genomics of Complex Diseases, Imperial College, London, United Kingdom

Corresponding author: Tuulia Varanka-Ruuska, Center for Life Course Health Research, P.O. Box 5000, 90014

University of Oulu, Oulu, Finland

Email: tuulia.varanka-ruuska@oulu.fi

Telephone: +358406744525

Fax: +35885375661

Revised manuscript, including author names, no track changes Click here to download Revised manuscript, including author names, no track changes Article with author names.docx

Introduction

Employment is a cultural yardstick, whereby people measure themselves in their society (Dodu 2005), and also a major determinant of the socioeconomic gradient in health (Waddell and Burton 2006). Unemployment, in turn, isolates a person from both material and immaterial gains related to working life, and has been linked with several aspects of poor health, such as self-rated health (Vaalavuo 2015; Broom et al. 2006; Giatti et al. 2010), increased risk for obesity and weight gain (Janlert 1997; Khlat et al. 2004; Montgomery et al. 1998; Laitinen et al. 2002), inflammation (Hughes et al. 2015), poor mental health (Artazcoz et al. 2004; Ford et al. 2010), hypertension (Janlert 1992), cardiovascular diseases (Lundin et al. 2014) and higher mortality (Roelfs DJ et al. 2011; Martikainen 1990; Martikainen and Valkonen 1996; Garcy and Vågerö 2012; Vågerö and Garcy 2016). However, although several risk factors of type 2 diabetes (T2D) have thus been addressed, the potential direct association between unemployment and disorders of glucose metabolism remains unanswered.

The incidence of T2D is increasing worldwide, imposing a major burden upon public health and economies (Seuring et al. 2015). T2D results from complex genetic-environmental interaction (Noble et al. 2011). Several risk factors for T2D have been documented such as older age, family history of T2D, ethnicity, obesity, physical inactivity, unhealthy diet, smoking, hypercholesterolemia and hypertension (Noble et al. 2011). T2D may develop through a long-term asymptomatic period, during which the prediabetic states, defined as impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), can be estimated by measuring glucose concentrations (Tabák et al. 2012). Fortunately, the diabetic cascade may be delayed and the development of T2D even prevented by changes in lifestyle including healthy diet and physical activity (Tuomilehto et al. 2001; Knowler et al. 2002; Lindström et al. 2013). The detecting of these phases to enable timely prevention remains a challenge (Noble et al. 2011), and it has been estimated that one of two adults with T2D are currently undiagnosed (International Diabetes Federation 2015). Critically, since the incidence of T2D is peaking in the working age between 40 and 59 years (Centers for Disease Control and Prevention 2015), it is important to recognize potential risk factors related to working life. Several employment-related factors, such as shift work (Eriksson et al. 2013; Morikawa et al. 2005), working overtime (Tayama et al. 2016), work-related stress (Novak et al. 2013), job insecurity (Ferrie et al. 2016; Virtanen et al. 2014) and low occupational class (Kumari et al. 2004; Heden Stahl et al. 2014) have been shown to associate with the risk of T2D. In contrast, the association of the widely prevalent (OECD 2014a) unemployment with T2D remains unsatisfactorily understood. This may result from unclear classification of nonworkers in the occupation-based measures of socioeconomic status, thus ignoring unemployment, a potentially stressful situation when an individual is lacking work yet willing and capable to work.

With the present study we aimed to summarize the published evidence from the last two decades concerning the associations between unemployment and disorders of glucose metabolism in population-based studies. Our hypothesis was that unemployment, a major stressor in the working age, is a risk factor of developing T2D, thereby associated with higher prevalence of prediabetes and diabetes. Regarding the internationally differing labor market patterns, especially the gendered differences regarding overall participation in the working life and in the distributions across occupations, we aimed to conduct a systematic review covering all population-based studies, followed by meta-analyses in unselected general population studies and further stratified for sex whenever possible.

Methods

Literature search

We planned the search and the analysis of the literature according to the MOOSE (meta-analysis of observational studies in epidemiology) guidelines (Stroup et al. 2000). The literature search was carried out by the first author with the help of an information specialist from three different databases: Scopus, Medline Ovid and Web of Science.

The search included keywords related to employment such as 'employment', 'unemployment', 'jobless' or 'job loss', and keywords concerning disorders and measures of glucose metabolism such as 'type 2 diabetes', 'gestational diabetes', 'prediabetes' or 'hyperglycemia', 'glucose intolerance' or 'glucose tolerance' or ´glucose impairment´. The search strategy and keywords are presented in detail in Appendix 1 (Online resource 1). The search was performed on the titles, abstracts and keywords of the published articles dating from the 1 January 1995 until the 20 October 2016. In addition, hand searching was performed on the reference lists of all articles selected for systematic review and non-systematically on other sources. In cases of incomplete information in the articles found, the authors of the articles were contacted via e-mail, eventually with one reminder, to provide more details. The flowchart of the search is shown in Figure 1.

Inclusion criteria

We included any population-based studies on unemployment in relation to glucose metabolism in the narrative systematic review. Respecting the anticipated heterogeneity of employment patterns across the subgroups of populations, only studies conducted in unselected general population samples were included in the quantitative meta-analysis.

We only included studies where we could identify the unemployed individuals from the other participants. We did not set further criteria regarding the duration or recurrence of unemployment. As outcomes of impaired glucose metabolism we considered gestational diabetes, prediabetes or T2D, covering all phases of the diabetic cascade. We included studies with any type of definition of these outcomes, including self-reported or register-based diagnosis or treatment of gestational diabetes or T2D, or diagnosis settled by laboratory tests, such as fasting plasma glucose (FPG), oral glucose tolerance test (OGTT), or glycated hemoglobin (HbA1c). We accepted studies with both cross-sectional and follow-up study designs.

Exclusion criteria

We excluded studies with unclear information on employment status, not allowing for distinguishing the unemployed individuals from the other participants. For example, we excluded studies which only roughly classified workers versus non-workers, implying that "non-workers" might have included homemakers, students or retired individuals not actively seeking for a job. Analogously, an exclusion criteria was lacking information of gestational diabetes, prediabetes or T2D.

Since the prevalence or incidence of unemployment among persons with diabetes was not in our focus, we excluded studies conducted among diabetic patients only. From the meta-analysis, we further excluded studies with overlapping or insufficient data, or conducted in non-general subpopulations. As a final criteria, we restricted our search in original articles written in English.

Variables

Unemployment: We defined those unemployed as lacking work but belonging to the labor force, i.e. capable and willing to work and searching for a salaried job (OECD 2014a). We accepted both self-reported and register-based measures, dichotomized as unemployment yes/no in the analyses.

Prediabetes, defined as IFG or/and IGT, could be diagnosed by measurements of fasting plasma/serum glucose and/or OGTT, or glycated hemoglobin (HbA1c). For IFG diagnosis, different criteria exist and were

accepted, such as FPG between 5.6 and 6.9 mmol/l according to American Diabetes Association's (ADA 2014) criteria and between 6.1-6.9 mmol/l by World Health Organization's (WHO 1999) criteria. In OGTT, a two hour plasma glucose between 7.8 mmol/l and 11.0 mmol/l indicated IGT (ADA 2014, WHO 1999). By HbA1c, prediabetes could be defined as value from 39 mmol/mol to 46 mmol/mol (ADA 2014). For analysis, these variables were then dichotomized as prediabetes yes/no, regardless of the type of the measurement.

Gestational diabetes: Gestational diabetes could be defined as self-reported diagnosis or treatment, or based on measured FPG or OGTT. If FPG was between 5.1 and 6.9 mmol/l, or in OGTT 1 hour glucose over 10.0 mmol/l, or 2 hour glucose between 8.5 and 11.0 mg/dl, defined as gestational diabetes (WHO 2013).

T2D could be defined as self-reported or register-based diagnosis, self-reported or register-based use of anti-diabetic medication, or diagnosis based on measured glucose concentrations. We accepted different classifications in defining T2D, also an age-based categorization of registered incident cases of diabetes, categorized as T2D if occurring at over 30 years of age and type 1 diabetes if occurring at earlier age. If based on measured glucose, the T2D diagnosis was defined through FPG over 7.0 mmol/l, glucose concentrations over 11.0 mmol/l in postprandial glucose samples or in 2-hour sample in OGTT after ingesting 75 g of glucose (or carbohydrates equivalent to this dose), or HbA1c over 46 mmol/mol.

For analysis, these variables were then dichotomized as T2D yes/no, regardless of the type of the measurement (WHO 1999, ADA 2014) Study selection First, based on the titles and the abstracts of the articles found, the first two authors independently selected the publications for further reading. Second, the full texts of the selected articles were retrieved and carefully read, to evaluate whether they met the inclusion criteria. These two authors compared and discussed their evaluations aiming to achieve consensus. Possible disagreements were planned to be settled through mutual discussion with the last author. The flow of the study selection is presented in Figure 1.

Quality assessment

We constructed a checklist, modified from a previous recommendation (Downs and Black 1998), for assessing the quality of the articles with 12 predefined items (Appendix 2, Online resource 2) related to conventional reporting and methodological practices in scientific articles. One item concerning confounders could receive 0-2 points, other items yielded 0-1 point each. The first two authors independently gave their ratings according to the checklist and discussed for consensus.

Analysis

For systematic review, we constructed a table with data fields to the designs, the characteristics and the reported results of the included population-based studies regarding unemployment and glucose metabolism. We also calculated the unemployment rates for each study as the percentages of unemployed individuals of the total labor force, where the latter consists of all unemployed, employed and self-employed individuals (OECD 2014a). Likewise, we uniformly calculated the prevalences or cumulative incidences of prediabetes and T2D for each study.

We prepared for quantitative analyses on the associations between unemployment and each outcome of glucose metabolism in the studies conducted in unselected general population samples, both in total samples and in the subgroups of men and women. For the meta-analysis, the following procedure was designed. Regarding the anticipated heterogeneity across the studies, random effects meta-analyses were chosen to calculate the odds ratios (ORs) and their 95% confidence intervals (CIs) for outcomes of glucose metabolism among those unemployed as compared to all employed individuals.

The heterogeneity of the studies was explored with the I2 statistic (with 95% CI), a recommended transformation of the Q statistic. Values of I2, ranging from 0% to 100%, reflect the proportion of the total

variation across studies beyond chance. Regarding quantity, 25% describes low, 50% moderate, and 75% high heterogeneity (Higgins et al. 2003). The statistical significance of this heterogeneity was tested using the chi-square test. We also planned to conduct an influence analysis in which the meta-analysis estimates are computed omitting one study at a time. To assess potential publication bias, Egger's test and funnel plots (Sterne 2009) were chosen. All statistical analyses were performed using STATA, version 13.1 (StataCorp LP, Texas, USA).

Results

Study selection

In total, the literature search retrieved 981 articles (Fig. 1). After screening titles and abstracts, or full texts if abstracts were missing, we retrieved 32 articles for further evaluation and selected nine articles to be reviewed and meta-analyzed. Hand searching yielded three articles, one of them by our own research group (Rautio et al. 2017), resulting in altogether 12 articles filling our criteria for systematic review.

Quality assessment

Overall quality was good ranging from 10 to 13 of potential 13 points. (Appendix 2, Online resource 2) Seven of the 12 quality assessment criteria were met by all of the studies included.

Study characteristics

Table 1 summarizes the 12 studies systematically reviewed: five studies from Europe, three from Near East, one from Asia, one from Australia, and two studies from Northern America. All but one (Martin et al. 2008) reported data for both sexes. The measurement of the employment status was based on self-reports in 10 studies, two studies used national registers (Poulsen et al. 2014, Rautio et al. 2017) (Table 1). In 11 of the 12 studies, unemployment status was determined at one time point, whereas one study used unemployment records during individually determined three-year follow-up periods preceding the OGTT date (Rautio et al. 2017).

Different methods for assessing glucose metabolism were found, as shown in Table 1. No study on gestational diabetes could be included due to unclear information on unemployment. Data on prediabetes was reported in six studies, four studies using OGTT and two studies using FPG. Regarding T2D diagnosis, five studies were based on both self-reports on diagnosis or anti-diabetic medication, and measurements of glucose concentrations. Three studies were based on selfreported T2D diagnoses only. Two studies only utilized laboratory tests. One study used only register-based diagnoses. Another one accepted several sources of information: registered data on diagnosis or on anti-diabetic medication or laboratory measurements of glucose concentrations. Nine studies were cross-sectional regarding measurement of glucose metabolism, and three studies had a longitudinal design, with known individuals with diabetes excluded at baseline and follow-up periods lasting from 5 to 12 years.

Reported results on unemployment and glucose metabolism in the articles The longitudinal study of Poulsen et al. (2014), was the only one to show a heightened risk (RR 2.13, 95% CI 2.06-2.21) for incident diabetes for the individuals unemployed at baseline during the 12-year follow-up, when using the group of professional employees as the reference category, even after adjustments for gender, age, country of origin and socioeconomic status (SES). In the study of Rautio et al. (2017), using a retrospective 3-year follow-up of unemployment records, the men who were unemployed for altogether >1 year (high exposure) had higher risk for prediabetes (OR 1.61, 95%CI 1.03-2.51), and screen-detected T2D (OR 2.58, 95%CI 1.23-5.44)

after adjustment for education, smoking, alcohol intake, physical activity and BMI. Among men with lower exposure (= 1 year) to unemployment, no significant association was found, not either among women.

In six of the 12 studies, unemployed individuals did not have higher risk for glucose metabolism disorders. Regarding all studies included in the narrative review, the reported results of unemployment with prediabetes and T2D are shown in Table 1, with largely differing reference groups across the studies.

Calculated unemployment rates

Evident typing errors in the articles concerning the reported numbers of unemployed were corrected in two cases, with replacement of new numbers provided by the authors (Ramezankhani et al. 2014) or a re-calculation based on the descriptive tables (Azimi-Nezhad et al. 2008), as detailed in Table 2. In sum, the calculated unemployment rates varied from 3.5 % in a Danish nationwide sample (Poulsen et al. 2014) to as high as 50.0 % within an ethnic group of Chaldean origin in the United States of America (Kridli et al. 2006).

Calculated prevalences and cumulative indexes of the disorders of glucose metabolism in the studies

Prevalence of prediabetes varied from 2.5% (Azimi-Nezhad et al. 2008) to 32.1% (Kridli et al. 2006). With varying sources of information, the calculated prevalence of T2D varied from 3.0% (Rautio et al. 2017) to 32.1% (Kridli et al. 2006). Calculated sex-stratified prevalence of T2D varied from 4.3% for men and 2.0% for women at lowest (Rautio et al. 2017) to 30.6% for men and 31.5% for women at highest (Kridli et al. 2006). In a five-year follow-up study in Iran with participants over 20 years of age, the calculated incidence of prediabetes was 10.5% and the corresponding figure for diabetes was 11.0% during the five years follow-up (Ramezankhani et al. 2014). A study in Germany, restricted to abdominally obese individuals aged 20-79, reported a T2D incidence of 7.7 % during the five years follow-up (Friedrich et al. 2013). A register-based study in Denmark covering the whole 30 - 59 years aged population recorded a 5.8% diabetes incidence during the 12 years follow-up (Poulsen et al. 2014).

Meta-analyses

Four studies in the systematic review had to be left out of the meta-analyses, due to insufficient descriptive data (Bird et al. 2015), to overlapping data (Müller et al. 2013b) and to non-general study populations restricted to a specific ethnic group (Kridli et al. 2006) or to individuals with abdominal obesity (Friedrich et al. 2013). The meta-analysis was thus based on eight studies. However, due to the small number of studies, sex-separated analyses were not conducted concerning prediabetes.

Unemployment and prediabetes

Figure 2 shows the calculated prevalences of prediabetes among the unemployed and the employed individuals and the odds ratio for prediabetes among the unemployed as compared to all employed. Across the five included studies, two studies showed heightened odds for prediabetes among the unemployed. The meta-analysis of the overall association yielded a 1.6-fold association of unemployment with prediabetes (OR 1.58; 95% CI 1.07-2.35). The heterogeneity of these studies was high (I^2= 91%; p=0.000).

Unemployment and T2D

Figure 3 shows the calculated prevalences of T2D among the unemployed and the employed and the ORs for T2D among the unemployed in all studies eligible for meta-analysis, with seven studies including both sexes, one only men (Martin et al. 2008). In six of the eight studies, the odds for T2D were significantly heightened among the unemployed and according to the meta-analysis in the total sample, the unemployed had 1.7-fold odds for T2D when compared to all employed individuals (OR 1.72; 95% CI 1.14-2.58). The heterogeneity of these studies was high (I^2= 99.3%; p=0.000).

Figure 4 shows the results of the corresponding subgroup analyses for men and women. Among men, the OR for T2D among the unemployed was 1.53 (95% CI 1.47-1.60) as compared to those employed. Among women, the corresponding figure was 1.60 (95%CI 1.33-1.92), respectively.

The aforementioned significant heterogeneity between the studies regarding unemployment and T2D (I2=99.3%, p=0.001) notably decreased when men and women were studied separately (I2=0.0%, p=0.503 for men and I2=36.5%, p=0.178 for women).

Tests for bias

In the influence study concerning the meta-analysis of unemployment and T2D in the total sample, the ORs were not statistically significantly affected when one study at a time was excluded. All ORs ranged between 1.5-1.9 and stayed within the confidence interval of the pooled OR. According to the Funnel plot and Egger's test (t=0.05, p=0.959), there was no indication of publication bias (Fig. 5). Due to the small the numbers of eligible studies, the corresponding analyses were not conducted for prediabetes nor for the sex-stratified analyses for diabetes.

Discussion

According to this meta-analysis, unemployment, a common adversity in labor market, is associated with disorders of glucose metabolism. The unemployed individuals had 1.6-fold odds for prediabetes and 1.7-fold odds for T2D as compared to all employed individuals. The corresponding sex-stratified odds for T2D were 1.5-fold among unemployed men, and 1.6-fold among women. Our finding adds to the body of literature linking unemployment and poor health (Artazcoz et al. 2004; Lundin et al. 2014; Roelfs DJ et al. 2011; Martikainen 1990; Martikainen and Valkonen 1996; Garcy and Vågerö 2012; Vågerö and Garcy 2016) with an important outcome, T2D, a growing global public health concern, with notable potential for prevention.

Despite the highly heterogeneous labor market patterns, unemployment is common worldwide, thereby a notable potential stressor in the working age. In year 2014, the global unemployment rate was 5.9% (OECD 2014a). The overall national prevalences varied from 3.5% in Korea to 26.3% in Greece (OECD 2014a), with large variation across specific groups, like foreign born individuals (OECD 2014b). In the studies included in this review, the calculated unemployment rates were well in line with those found in the global statistics, varying from 3.5% to 24.4%, with one outlier reporting as high as 50.0% unemployment rate within a specific ethnicity-based sample (Kridli et al. 2006) and thereby excluded from the meta-analysis restricted to unselected general population samples.

Importantly, the participation of women in working life greatly varies internationally: in many countries of Europe and China over 40% of the total labor force is female, in the Near- and Middle-East the corresponding figure is below 20% (World Bank 2016). This was reflected also in the studies included in our review, in that the calculated proportion of women as homemakers was 86.2% in Iran at highest (Al-Baghli et al. 2010). The pressure towards women's participation in the working life and the perceptions of meaning of unemployment may vary culturally. Nevertheless, we found unemployment rates to be the higher among women than men in five of the six studies where sex-specific data were available. Despite these observed differences in women's participation in the labor market between the countries, in the meta-analyses we didn't detect significant differences between men and women regarding the association of unemployment with T2D.

Regarding the mechanisms behind the findings, it is evident, that the health behaviors and the extent to which unemployment is perceived as a stressor may have differed between the study populations in this

review. Unfortunately, the adjustment protocols widely varied as not even adjustments for age were performed in all studies. Therefore, further meta-regression analyses could not be conducted to analyze the potential underlying factors behind the observed associations.

There are several potential sources of bias behind the reported association within the individual studies. Selection bias may have resulted from the uneven distribution of unemployment by sex, ethnicity, local employment patterns or cultural issues, but also from selection to unemployment as a result of poor health. In observational studies, uncontrolled confounding always remains a possibility. Moreover, classification biases may have originated from the heterogeneous measures of unemployment and glucose metabolism. Regarding the review, biases may results from not reaching all relevant studies and from the always possible publication bias.

Diabetes with related health problems may be at least a partial reason for unemployment, but unfortunately the quantity of the potential reversed causality cannot be assessed. In line with this reasoning however, the calculated unemployment rate was higher (21.7%) among abdominally obese employees (Friedrich et al. 2013) than among the unselected general population sample (18.8%) in the same year in the same country (Müller et al. 2013a,b). The prevalence of unemployment among those with poorer health may also be affected by national policies and economic cycles. In the study by Zhang et al. (2013) the authors discussed that the recently implemented early retirement policy for unhealthy persons in China might have explained the higher odds of diabetes among retired people and therefore underestimated the significance of unemployment.

We note that 11 out of the 12 studies in our review measured unemployment only cross-sectionally, although the number of unemployment periods and the length of unemployment preceding the measurement could have varied from a few days to years of unemployment. The body of the current evidence suggests that the accumulation of one or more previous periods of unemployment correlates with deteriorated health and health behavior (Janlert et al. 2015; Garcy and Vågerö 2012; Vågerö and Garcy 2016). This pattern was also seen in the study of Rautio et al. (2017) considering the level of exposure to unemployment during three years, where the risk for disorders of glucose metabolism was significantly heightened when exposure to unemployment exceeded 1 year (1.6-fold risk for screen detected rediabetes, 2.6-fold for T2D) but not with lesser exposure.

With our exclusion criteria concerning unemployment, we sought to ensure good quality in defining the exposure to unemployment. The choice of comparing the unemployed to all employed individuals was considered the most applicable to summarize the data in the varying designs in this meta-analysis. The results reported in the articles therefore differed from the ones calculated in this study. For example, the largest register-based longitudinal study covering the whole Danish working-age population found over 2-fold risk for T2D (RR 2.13; 95%CI 2.06-2.21) among the unemployed, when compared to the group of professional individuals and adjusted for gender, age, country of origin and socioeconomic status (Poulsen et al. 2014). In contrast, when we determined all employed individuals as the reference category within the same data, the OR was 1.48 (95% CI 1.44-1.52) in the unadjusted analysis.

The assessment of glucose metabolism varied widely in the included studies, implying a potential source of classification bias, especially in terms of prediabetes. Noteworthly, it has been questioned whether the term prediabetes should be replaced, for example, with impaired glucose metabolism, in light of evidence showing that only 5-10 % of people with prediabetes per year will progress into T2D (Tabak et al. 2012). Nevertheless, regarding the long term development of diabetes and the evidence that even half of the individuals with T2D are unrecognized, the cross-sectional measures of T2D may have led to underestimations of T2D prevalence.

The small number of studies that met the inclusion criteria for the review raises concerns of a potential bias, also including only studies published in English may have left out potential important uncovered studies. Nevertheless, covering all continents except Africa and South America, the global representativeness of the included studies appeared reasonable, and the possibility of outcome reporting bias was reduced by contacting authors for their unpublished data. There was large heterogeneity in the sample sizes, ranging from over 200 to over 2 million individuals. By the quality assessment criteria the overall quality of the included studies was good.

In sum, the main challenge in synthesizing the results is the heterogeneity of the studies. Therefore, studies conducted within specific subpopulations (Friedrich et al. 2013, Kridli et al. 2006) were only included in the systematic review and excluded from the meta-analyses. In the meta-analyses, we expectedly found significant heterogeneity in the studies concerning the total sample, which however decreased when men and women were studied separately. Nevertheless, the main result of the meta-analysis persisted in the influence test, and no indication of publication bias was found according to Egger's test.

For practitioners in the health care sector, various screening tools have been designed to improve the early detection and the results of treatment of diabetes, further supporting the aims of secondary and tertiary prevention of various complications of diabetes (Noble et al. 2011). However, the implementation of such screening tools has turned out to be difficult (Dhippayom et al. 2014). Beyond screening, the improvement of patient outcomes may also require novel integrated social and health policies and tailored care for subgroups at higher risk (Noble et al. 2011). Our results highlight the subgroup of unemployed people. Thus, the feasibility and efficacy of considering unemployment history as a risk factor for T2D should be evaluated in further trials in various levels of health care. At present, the high prevalence and incidence of prediabetes and T2D in the working aged population as well as the high prevalence of unemployment emphasize the relevance of this finding, observed in different labor market settings, and both among men and women.

Conclusions

To the best of our knowledge, this is the first meta-analysis based on a systematic review suggesting an association between unemployment and disorders of glucose metabolism, with 1.6.-fold odds for prediabetes and 1.7-fold odds for T2D among the unemployed as compared to those employed. The association seems identical in both men and women and appears to be observed in different labor market settings internationally. Since the factors underpinning the association were not systematically addressed in the reviewed studies, the numerous potential mediating and confounding factors need to be tested in further research.

Compliance with ethical standards

This article is based on a secondary analysis of existing literature and does not contain any studies with human participants nor animals conducted by the authors. Obtaining approval by an ethics committee is not required under national regulations. Good scientific standards have been followed according to MOOSE guidelines.

Funding

This project has received funding from the Academy of Finland (#268336) and the European Union's Horizon 2020 research and innovation program (under grant agreement No 633595) for the DynaHEALTH action. The funders had no role in study design, data analysis, data interpretation and writing of the paper.

References

Al-Baghli NA, Al-Ghamdi AJ, Al-Turki KA, Al Elq AH, El-Zubaier AG, Bahnassy A (2010) Prevalence of diabetes mellitus and impaired fasting glucose levels in the Eastern Province of Saudi Arabia: Results of a screening campaign. Singapore Med J 51:923-930

American Diabetes Association (2014) Diagnosis and classification of diabetes mellitus. Diabetes Care 37 Supplement 1:S81-S90. doi.org/10.2337/dc14-S081

Artazcoz L, Benach J, Borrell C, Cortès I (2004) Unemployment and mental health: Understanding the interactions among gender, family roles, and social class. Am J Public Health 94:82-88

Azimi-Nezhad M, Ghayour-Mobarhan M, Parizadeh MR, Safarian M, Esmaeili H, Parizadeh SMJ, Khodaee G, Hosseini J, Abasalti Z, Hassankhani B, Ferns G (2008) Prevalence of type 2 diabetes mellitus in Iran and its relationship with gender, urbanisation, education, marital status and occupation. Singapore Med J 49:571-576

Bartley M (1994) Unemployment and ill health: understanding the relationship. J Epidemiol Community Health 48:333- 337

Bartley M, Owen C (1996) Relation between socioeconomic status, employment, and health during economic change, 1973-93. BMJ 313:445-449

Bird Y, Lemstra M, Rogers M, Moraros J (2015) The relationship between socioeconomic status/income and prevalence of diabetes and associated conditions: A cross-sectional population-based study in Saskatchewan, Canada. Intern j equity health 14:93. doi.org/10.1186/s12939-015-0237-0

Broom DH, D'Souza RM, Strazdins L, Butterworth P, Parslow R, Rodgers B (2006) The lesser evil: bad jobs or unemployment? A survey of mid-aged Australians. Soc Sci Med 63:575-586

Centers for Disease Control and Prevention (2015). Distribution of age at diagnosis of diabetes among adult incident cases aged 18-79 years, United States, 2011. http://www.cdc.gov/diabetes/statistics/age/fig1.htm. Accessed 3 September 2015.

Dhippayom T, Chaiyakunapruk N, Krass I (2014) How diabetes risk assessment tools are implemented in practice: A systematic review. Diabetes Res Clin Pract 104:329-242. doi; 10.1016/j.diabres.2014.01.008

Dodu N (2005) Is employment good for well-being? A literature review. Journal of Occupational Psychology, Employment and Disability 7:17-33

Downs SH, Black N (1998) The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health 52:377-384

Eriksson AK, van den Donk M, Hilding A, Östenson CG (2013) Work stress, sense of coherence, and risk of type 2 diabetes in a prospective study of middle-aged Swedish men and women. Diabetes Care 36:2683-2689 doi;org/10.2337/dc12-1738

Ferrie JE, Virtanen M, Jokela M (2016) Job insecurity and risk of diabetes: a meta-analysis of individual participant data. CMAJ Canadian Medical Association Journal. DOI 10.1503/cmaj.150942

Ford E, Clark C, McManus S, Harris J, Jenkins R, Bebbington P, Brugha T, Meltzer H, Stansfeld SA (2010) Common mental disorders, unemployment and welfare benefits in England. Public Health 124:675-681. doi;10.1016/j.puhe.2010.08.019

Friedrich N, Schneider HJ, John U, Dörr M, Baumeister SE, Homuth G, Völker U, Wallaschofski H (2013) Correlates of adverse outcomes in abdominally obese individuals: Findings from the five-year followup of the population-based study of health in Pomerania. J Obes 2013. doi;10.1155/2013/762012

Garcy AM, Vågerö D (2012) The length of unemployment predicts mortality, differently in men and women, and by cause of death: A six year mortality follow-up of the Swedish 1992-1996 recession. Soc Sci Med 74:1911-1920. doi;10.1016/j.socscimed.2012.01.034

Giatti L, Barreto SM, César CC (2010) Unemployment and self-rated health: Neighborhood influence. Soc Sci Med 71:815-823. doi.org/10.1016/j.socscimed.2010.05.021

Heden Stahl C, Novak M, Hansson P, Lappas G, Wilhelmsen L, Rosengren A (2014) Incidence of type 2 diabetes among occupational classes in Sweden: a 35-year follow-up cohort study in middle-aged men. Diabetic Med 31:674- 680

Higgins J, Thompson S, Deeks J, Altman (2003) Measuring inconsistency in meta-analyses. BMJ : British Medical Journal 327:557-–560

Hughes A, McMunn A, Bartley M, Kumari M (2015) Elevated inflammatory biomarkers during unemployment: modification by age and country in the UK. Journal of epidemiology and community health 69:673-679. doi;10.1136/jech-2014-204404

International Diabetes Federation (2015) .IDF Diabetes Atlas, 7th edn. Brussels, Belgium: International Diabetes Federation

Janlert U (1992) Unemployment and blood pressure in Swedish building labourers. Journal of Internal Medicine 231:241-246

Janlert U (1997) Unemployment as a disease and diseases of the unemployed. Scand J Work Environ Health 23:79-83

Janlert U, Winefield AH, Hammarstrom A (2015) Length of unemployment and health-related outcomes: a life-course analysis. Eur J Public Health 25:662-667. doi;10.1093/eurpub/cku186

Khlat M, Sermet C, Le Pape A (2004) Increased prevalence of depression, smoking, heavy drinking and use of psychoactive drugs among unemployed men in France. Eur J Epidemiol 19:445-451. doi;10.1023/B:EJEP.0000027356.71414.bd

Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM (2002) Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. New Engl J Med 346:393-403. doi;10.1056/NEJMoa012512

Kridli SA-, Herman WH, Brown MB, Fakhouri H, Jaber LA (2006) The epidemiology of diabetes and its risk factors among Chaldean Americans. Ethn Dis 16:351-356

Kumari M, Head J, Marmot M (2004) Prospective study of social and other risk factors for incidence of type 2 diabetes in the Whitehall II study. Arch Intern Med 164:1873-1880

Laitinen J, Power C, Ek E, Sovio U, Järvelin MR (2002) Unemployment and obesity among young adults in a Northern Finland 1966 birth cohort. Int J Obes 26:1329-1338. doi;10.1038/sj.ijo.0802134

Lindström J, Peltonen M, Eriksson JG, Ilanne-Parikka P, Aunola S, Keinänen-Kiukaanniemi S, Uusitupa M, Tuomilehto J (2013) Improved lifestyle and decreased diabetes risk over 13 years: Long-term follow-up of the randomised Finnish Diabetes Prevention Study (DPS). Diabetologia 56:284-293

Lundin A, Falkstedt D, Lundberg I, Hemmingsson T (2014) Unemployment and coronary heart disease among middleaged men in Sweden: 39 243 men followed for 8 years. Occup Environ Med 71:183-188. doi;10.1136/oemed-2013- 101721

Martikainen PT (1990) Unemployment and mortality among Finnish men, 1981-5. Br Med J 301:407-411

Martikainen PT, Valkonen T (1996) Excess mortality of unemployed men and women during a period of rapidly increasing unemployment. Lancet 348:909-912. doi;10.1016/S0140-6736(96)03291-6

Martin SA, Haren MT, Taylor AW, Middleton SM, Wittert GA (2008) Chronic disease prevalence and associations in a cohort of Australian men: The Florey Adelaide Male Ageing Study (FAMAS). BMC Public Health 8. doi;10.1186/1471-2458-8-261

Morikawa Y, Nakagawa H, Miura K, Soyama Y, Ishizaki M, Kido T, Naruse Y, Suwazono Y, Nogawa K (2005) Shift work and the risk of diabetes mellitus among Japanese male factory workers. Scand J Work Environ Health:179-183

Müller G, Hartwig S, Greiser KH, Moebus S, Pundt N, Schipf S, Völzke H, Maier W, Meisinger C, Tamayo T, Rathmann W, Berger K (2013a) Gender differences in the association of individual social class and neighbourhood unemployment rate with prevalent type 2 diabetes mellitus: A cross-sectional study from the DIAB-CORE consortium. BMJ Open 3. doi;10.1136/bmjopen-2013-002601

Müller G, Kluttig A, Greiser KH, Moebus S, Slomiany U, Schipf S, Völzke H, Maier W, Meisinger C, Tamayo T, Rathmann W, Berger K (2013b) Regional and neighborhood disparities in the odds of type 2 diabetes: Results from 5 population-based studies in Germany (DIAB-CORE consortium). Am J Epidemiol 178:221-230. doi;10.1093/aje/kws466

Noble D, Mathur R, Dent T, Meads C, Greenhalgh T (2011) Risk models and scores for type 2 diabetes: Systematic review. BMJ (Online) 343:1243. doi;10.1136/bmj.d7163

Novak M, Björck L, Giang KW, Heden-Ståhl C, Wilhelmsen L, Rosengren A (2013) Perceived stress and incidence of type 2 diabetes: A 35-year follow-up study of middle-aged Swedish men. Diabetic Med 30:e8-e16

OECD (2014a) Unemployment rate. doi;10.1787/997c8750-en

OECD (2014b) Employment and unemployment rates by gender and place of birth. doi;10.1787/data-00722-en

Poulsen K, Cleal B, Willaing I (2014) Diabetes and work: 12-year national follow-up study of the association of diabetes incidence with socioeconomic group, age, gender and country of origin. Scand J Public Health 42:728-733. doi;10.1177/1403494814556177

Ramezankhani A, Pournik O, Shahrabi J, Khalili D, Azizi F, Hadaegh F (2014) Applying decision tree for identification of a low risk population for type 2 diabetes. Tehran lipid and glucose study. Diabetes Res Clin Pract. doi;10.1016/j.diabres.2014.07.003

Rautio N, Varanka-Ruuska T, Vaaramo E, Palaniswamy S, Nedelec R, Miettunen J, Karppinen J, Auvinen J, Järvelin M, Keinänen-Kiukaanniemi S, Sebert S, Ala-Mursula L (2017). Accumulated exposure to unemployment is related to impared glucose metabolism in middle-aged men: a follow-up of the Northern Finland Birth Cohort 1966. Primary Care Diabetes doi.org/10.1016/j.pcd.2017.03.010

Roelfs DJ, Shor E, Davidson KW, Schwartz JE (2011) Losing life and livelihood: a systematic review and metaanalysis of unemployment and all-cause mortality. Soc Sci Med 72:840-854. doi;org/10.1016/j.socscimed.2011.01.005

Seuring T, Archangelidi O, Suhrcke M (2015) The economic costs of type 2 diabetes: A global systematic review. Pharmacoeconomics 33:811-831. doi;10.1007/s40273-015-0268-9

Sterne J (2009) Meta-analysis in Stata: An updated collection from The Stata Journal| Jonathan Sterne| 9781597180498| CRC PRESS.

Stroup D, Berlin J, Morton S (2000) Meta-analysis of observational studies in epidemiology A proposal for reporting. Journal of the American Medical Association 283:2008-2012

Tabák AG, Herder C, Rathmann W, Brunner EJ, Kivimäki M (2012) Prediabetes: a high-risk state for diabetes development. The Lancet 379:2279-2290

Tayama J, Li J, Munakata M (2016) Working long hours is associated with higher prevalence of diabetes in urban male Chinese workers: The Rosai Karoshi Study. Stress Health 32:84-87. doi;10.1002/smi.2580

Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, Keinänen-Kiukaanniemi S, Laakso M, Louheranta A, Rastas M, Salminen V, Uusitupa M (2001) Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. New Engl J Med 344:1343-1350. doi;10.1056/NEJM200105033441801

Vaalavuo M (2015) Deterioration in health: What is the role of unemployment and poverty? Scand J Public Health 44:347-353. doi;10.1177/1403494815623654

Virtanen M, Ferrie JE, Tabak AG, Akbaraly TN, Vahtera J, Singh-Manoux A, Kivimäki M (2014) Psychological distress and incidence of type 2 diabetes in high-risk and low-risk populations: The Whitehall II cohort study. Diabetes Care 37:2091-2097. doi;10.2337/dc13-2725

Vågerö D, Garcy AM (2016) Does unemployment cause long-term mortality? Selection and causation after the 1992-96 deep Swedish recession. Eur J Public Health. doi;org/10.1093/eurpub/ckw053

Waddell G, Burton KA (2006) Is work good for your health and well-being? TSO, London, UK World Bank (2016) Labor force participation rate, female (% of female population ages 15+) (modeled ILO estimate). http://data.worldbank.org/indicator/SL.TLF.CACT.FE.ZS. Accessed 28 November 2016

World Health Organization (1999) Definition, diagnosis and classification of diabetes mellitus and its complication. Report of a WHO consultation. Part 1: Diagnosis and classification of diabetes mellitus. World Health Organization, Geneva, Report No 99.2

World Health Organization (2013) Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy

Zhang H, Xu W, Dahl AK, Xu Z, Wang H-X, Qi X (2013) Relation of socio-economic status to impaired fasting glucose and type 2 diabetes: Findings based on a large population-based cross-sectional study in Tianjin, China. Diabet Med 30:e157-e162. doi;10.1111/dme.12156

Titles for figures and tables in the order they appear in the manuscript

I: Fig. 1

Flowchart of study selection

II: Table 1

Characteristics of the studies included in the systematic review. The results concerning unemployment and disorders of glucose metabolism are reported as available in the articles, the calculated unemployment rate, and the calculated prevalence /cumulative incidence of type2 diabetes (T2D) and prediabetes

III: Fig. 2

Calculated prevalence (%) of prediabetes among unemployed and all employed individuals, and odds ratios (OR) with their 95% confidence intervals (CI) for prediabetes among unemployed compared to employed individuals

IV: Fig. 3

Calculated prevalence (%) of type 2 diabetes (T2D) among unemployed and all employed individuals, and odds ratios (OR) with their 95% confidence intervals (CI) for T2D among unemployed compared to employed individuals

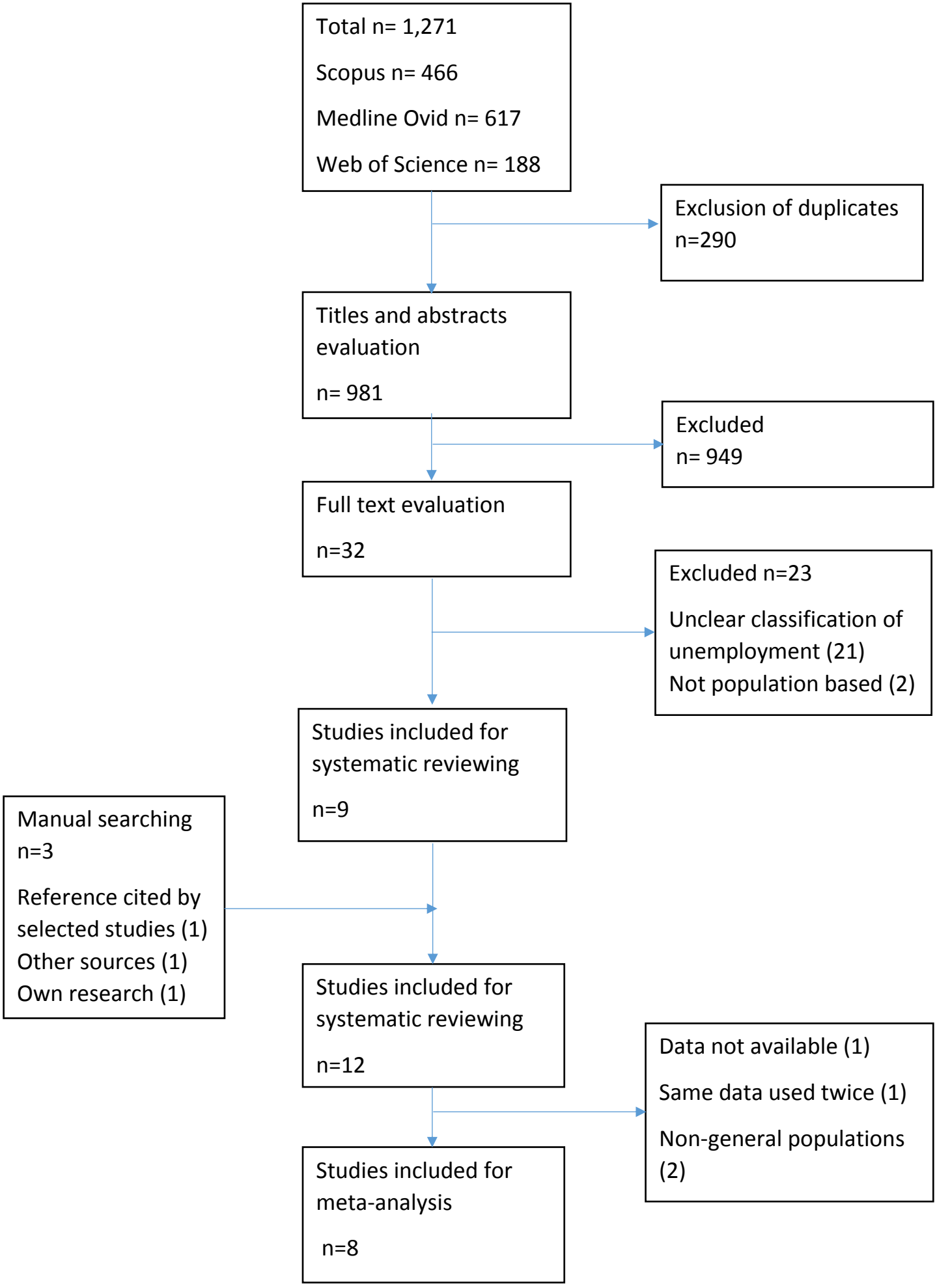
V: Fig. 4

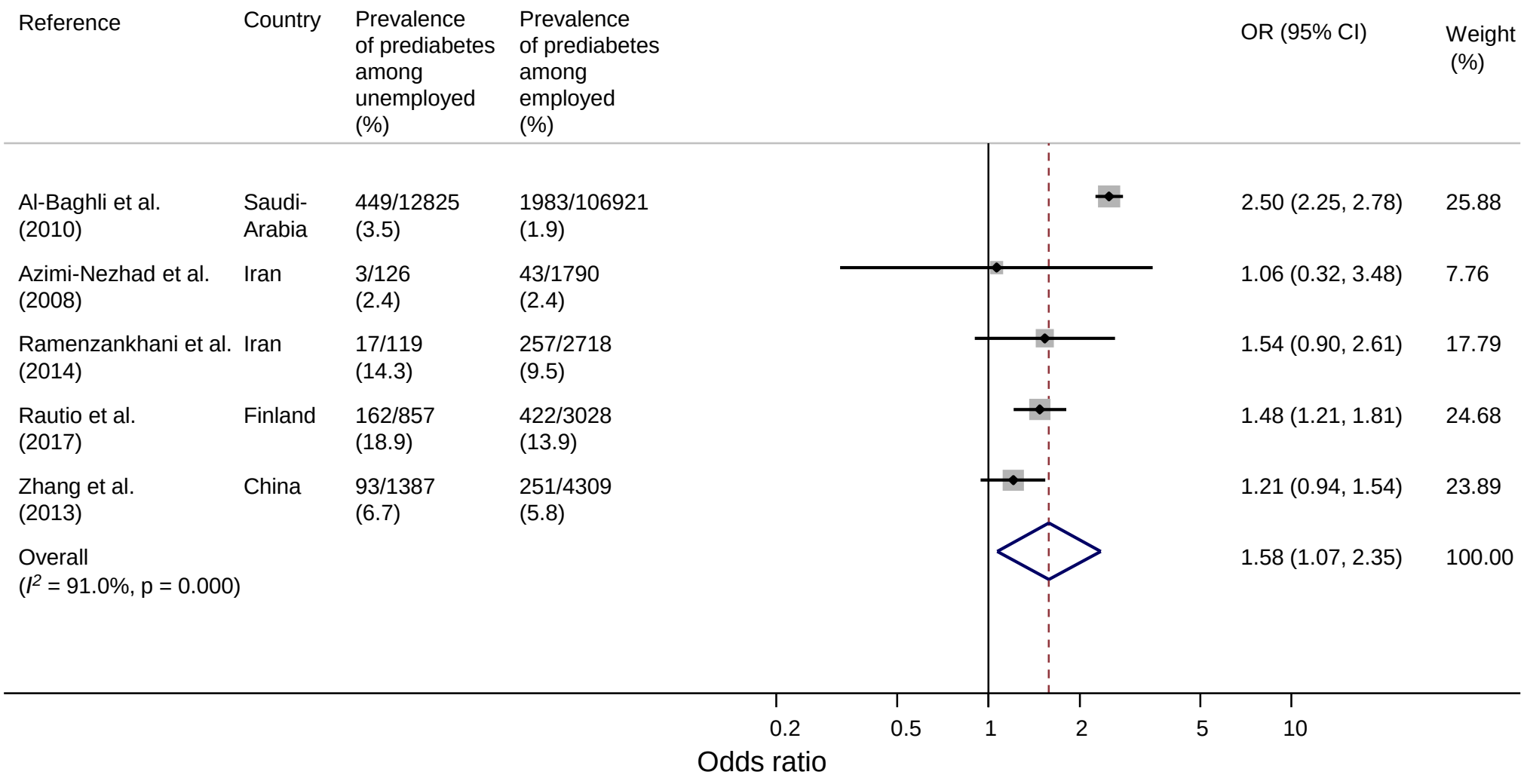
Calculated sex-separated prevalences (%) of type 2 diabetes (T2D) among unemployed and all employed individuals, and odds ratios (OR) with their 95% confidence intervals (CI) for T2D among unemployed compared to employed individuals

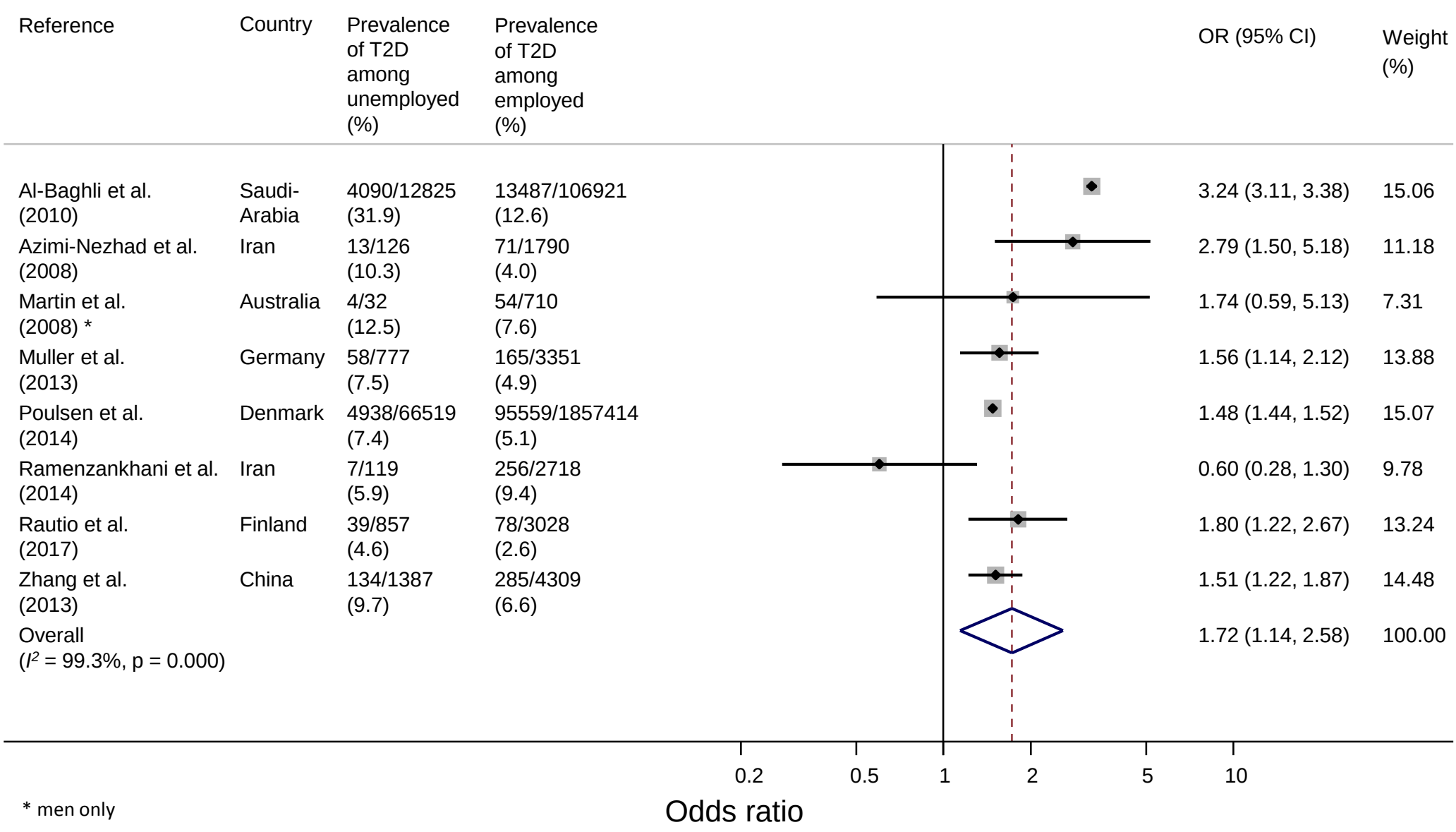
VI: Fig. 5

Funnel plot of studies included in meta-analysis for association between type 2 diabetes (T2D) and unemployment

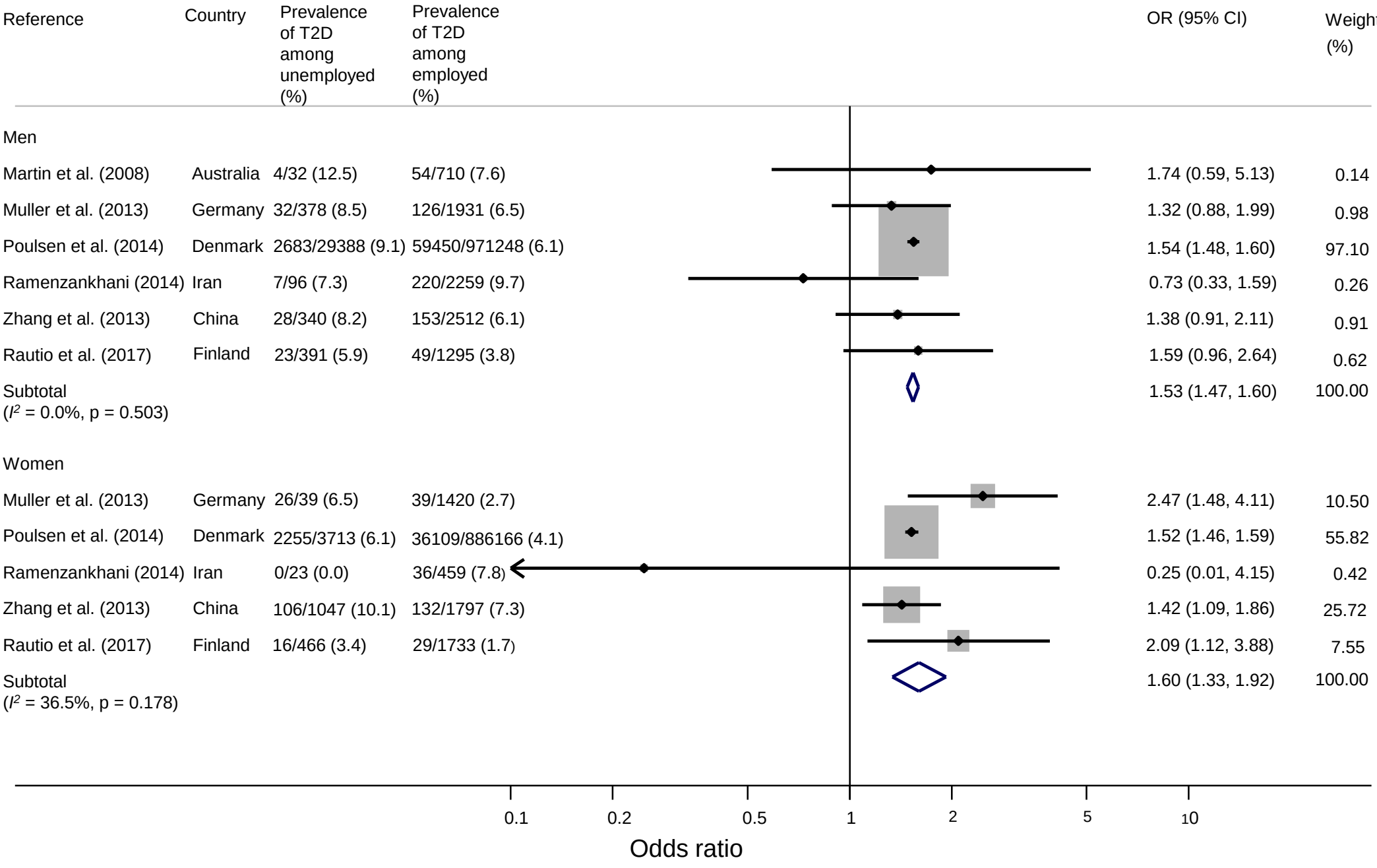
electronic supplemental material


Total n= 1,271
Scopus n= 466
Medline Ovid n= 617
Web of Science n= 188
Exclusion of duplicates n=290
Titles and abstracts evaluation
n= 981
Excluded
n= 949
Full text evaluation
n=32
Excluded n=23
Unclear classification of unemployment (21)
Not population based (2)
Studies included for systematic reviewing
n=9
Manual searching
n=3
Reference cited by selected studies (1)
Other sources (1)
Own research (1)
Studies included for systematic reviewing
n=12
Data not available (1)
Same data used twice (1)
Non-general populations (2)
Studies included for meta-analysis
n=8


Reference
Country
Prevalence of prediabetes among unemployed (%)
Prevalence of prediabetes among employed (%)
OR (95% CI)
Weight (%)
Al-Baghli et al. (2010)
Saudi-Arabia
449/12825 (3.5)
1983/106921 (1.9)
2.50 (2.25, 2.78)
25.88
Azimi-Nezhad et al. (2008)
Iran
3/126 (2.4)
43/1790 (2.4)
1.06 (0.32, 3.48)
7.76
Ramenzankhani et al. (2014)
Iran
17/119 (14.3)
257/2718 (9.5)
1.54 (0.90, 2.61)
17.79
Rautio et al. (2017)
Finland
162/857 (18.9)
422/3028 (13.9)
1.48 (1.21, 1.81)
24.68
Zhang et al. (2013)
China
93/1387 (6.7)
251/4309 (5.8)
1.21 (0.94, 1.54)
23.89
Overall
(I^2 = 91.0%, p = 0.000)
1.58 (1.07, 2.35)
100.00
0.2
0.5
1
2
5
10
Odds ratio


Reference
Country
Prevalence of T2D among unemployed (%)
Prevalence of T2D among employed (%)
OR (95% CI)
Weight (%)
Al-Baghli et al. (2010)
Saudi-Arabia
4090/12825 (31.9)
13487/106921 (12.6)
3.24 (3.11, 3.38)
15.06
Azimi-Nezhad et al. (2008)
Iran
13/126 (10.3)
71/1790 (4.0)
2.79 (1.50, 5.18)
11.18
Martin et al. (2008) *
Australia
4/32 (12.5)
54/710 (7.6)
1.74 (0.59, 5.13)
7.31
Muller et al. (2013)
Germany
58/777 (7.5)
165/3351 (4.9)
1.56 (1.14, 2.12)
13.88
Poulsen et al. (2014)
Denmark
4938/66519 (7.4)
95559/1857414 (5.1)
1.48 (1.44, 1.52)
15.07
Ramenzankhani et al. (2014)
Iran
7/119 (5.9)
256/2718 (9.4)
0.60 (0.28, 1.30)
9.78
Rautio et al. (2017)
Finland
39/857 (4.6)
78/3028 (2.6)
1.80 (1.22, 2.67)
13.24
Zhang et al. (2013)
China
134/1387 (9.7)
285/4309 (6.6)
1.51 (1.22, 1.87)
14.48
Overall (I^2 = 99.3%, p = 0.000)
1.72 (1.14, 2.58)
100.00
0.2
0.5
1
2
5
10
Odds ratio

* men only


Reference
Country
Prevalence of T2D among unemployed (%)
Prevalence of T2D among employed (%)
OR (95% CI)
Weight (%)
Men
Martin et al. (2008) Australia 4/32 (12.5) 54/710 (7.6) 1.74 (0.59, 5.13) 0.14
Muller et al. (2013) Germany 32/378 (8.5) 126/1931 (6.5) 1.32 (0.88, 1.99) 0.98
Poulsen et al. (2014) Denmark 2683/29388 (9.1) 59450/971248 (6.1) 1.54 (1.48, 1.60) 97.10
Ramenzankhani (2014) Iran 7/96 (7.3) 220/2259 (9.7) 0.73 (0.33, 1.59) 0.26
Zhang et al. (2013) China 28/340 (8.2) 153/2512 (6.1) 1.38 (0.91, 2.11) 0.91
Rautio et al. (2017) Finland 23/391 (5.9) 49/1295 (3.8) 1.59 (0.96, 2.64) 0.62
Subtotal (I^2 = 0.0%, p = 0.503) 1.53 (1.47, 1.60) 100.00
Women
Muller et al. (2013) Germany 26/39 (6.5) 39/1420 (2.7) 2.47 (1.48, 4.11) 10.50
Poulsen et al. (2014) Denmark 2255/3713 (6.1) 36109/886166 (4.1) 1.52 (1.46, 1.59) 55.82
Ramenzankhani (2014) Iran 0/23 (0.0) 36/459 (7.8) 0.25 (0.01, 4.15) 0.42
Zhang et al. (2013) China 106/1047 (10.1) 132/1797 (7.3) 1.42 (1.09, 1.86) 25.72
Rautio et al. (2017) Finland 16/466 (3.4) 29/1733 (1.7) 2.09 (1.12, 3.88) 7.55
Subtotal (I^2 = 36.5%, p = 0.178) 1.60 (1.33, 1.92) 100.00
0.1
0.2
0.5
1
2
5
10
Odds ratio

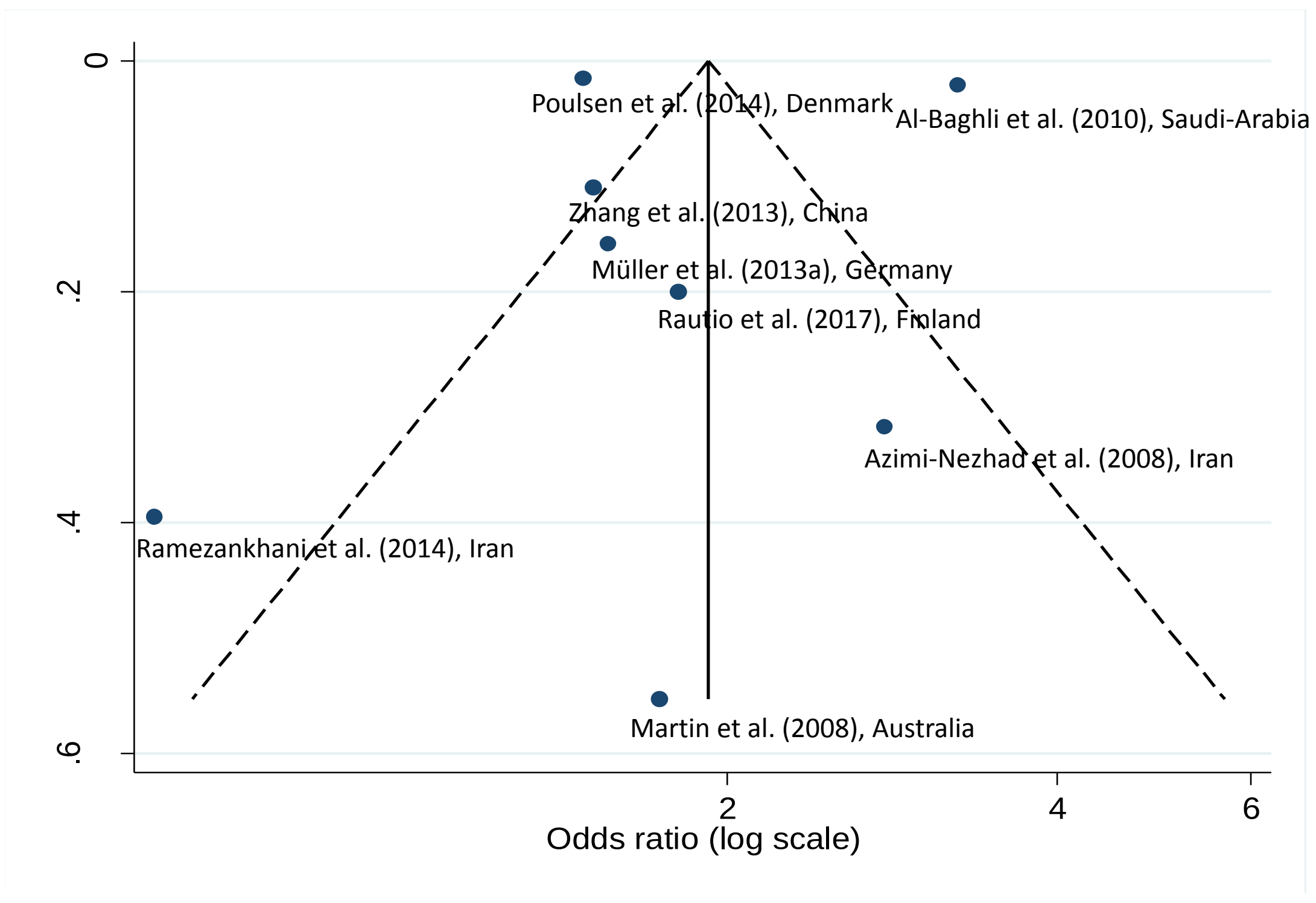

0
.2
.4
.6
Poulsen et al. (2014), Denmark
Al-Baghli et al. (2010), Saudi-Arabia
Zhang et al. (2013), China
Müller et al. (2013a), Germany
Rautio et al. (2017), Finland
Azimi-Nezhad et al. (2008), Iran
Ramezankhani et al. (2014), Iran
Martin et al. (2008), Australia
2
4
6
Odds ratio (log scale)

Table 1 Characteristics of the studies included in the systematic review

Reference, country	Study design (possible follow up-time)	Age, % of men, (other than population based study)	Sample size	Classification of employment (S = self reported, R =register based)	Assessment of glucose metabolism (S = self reported, M =measured, R =register based)	The reported results in the articles concerning unemployment and disorders of glucose metabolism (OR = odds ratio, RR = relative risk, CI = confidence interval)	Calculated unemployment rate [f]: Total Men Women	Calculated prevalence/ cumulative incidence of: T2D [g] T2D men T2D women Prediabetes
Al-Baghli et al. (2010), Saudi-Arabia	Cross-sectional	> 30 y, 51.7% men	197,681	S: Employed (military, professional, technical, non-technical, administration, self-employed), unemployed, not in workforce (housewife)	S: previous diagnosis of DM M: FCBG, CCBG and confirmed by FPG	Unemployed did not have higher risk for DM (OR 0.96; 95% CI 0.89 - 1.02) or IFG, (OR 1.14; CI 0.97-1.13) compared to self-employed (adjusted for age and sex). [b]	10.7% N/A N/A	17.3% N/A N/A 2.7%
Azimi-Nezhad et al. (2008), Iran	Cross-sectional	15 - 64 y, 49.1% men	3778	S: Employed (office or administrative worker, manual worker), unemployed, not in workforce (housewife, student, retired)	M: FSG	Prevalence of screen-detected DM 10.3% among unemployed, 3.2% administrative officers, 4.1% manual workers, 5.9% housewives, 0% students and 14.4% among retired (p<0.001). For IFG 2.4%, 3.2%,2.2%,2.5%,2.6% and 3.6% Occupation not related to DM (adjusted for age and sex). [b,c]	6.6% N/A N/A	5.5% 5.1% 5.8% 2.5%
Bird et al. (2015), Canada [a]	Cross-sectional	≥ 20 y, 44.1% men	27,090	S: Employed (part-time, full-time), unemployed	S: T2D	Prevalence of T2D 12.6% among unemployed, 5.1% part-time workers and 3.9% among full-time workers (p<0.001). Employment not related to T2D (adjusted for age). [b]	N/A	7.0% 7.7% 6.5%
Friedrich et al. (2013), Germany [a]	Follow-up study (5 y)	20 - 79 y, 58.3% men (abdominal obese)	1506	S: Employed, unemployed, not in workforce (retired)	S: T2D M: HbA1c	Unemployed obese individuals did not have higher risk for incident T2D (OR 1.03; 95% CI 0.53-1.97) compared to employed or retired (adjusted for age, sex and waist circumference). [b]	21.7% N/A N/A	7.7% N/A N/A

Kridli et al. (2006), USA [a]	Cross-sectional	≥ 20 y, 36.3% men (Chaldean Americans)	234	S: Employed (full-time, part-time), unemployed, not in workforce (homemaker, in school, retired, disabled, other)	S: previous diagnosis or medication of DM M: FPG, OGTT	Prevalence of DM 23.1% among unemployed men, 19.2% among full-time working men, 0% in part-time working men, 30.8% in retired men, 19.2% in disabled men, 0% in men who were still in school and 7.7% in homemaking men. For prevalence of IFG/IGT 29.6%, 37.0%, 14.8%, 7.4%, 7.4%, 0% and 3.7% (p=0.09). For women for prevalence of DM were 4.3%, 0%, 0%, 8.5%, 29.8%, 0% and 57.4%, and for IFG/IGT 17.3%, 3.8%, 5.8%, 3.8%, 21.1%, 0% and 48.1% (p<0.01).[b]	50.0% 39.2% 64.7%	31.2% 30.6% 31.5% 32.1%
Martin et al. (2008), Australia	Cross-sectional	35- 80 y, 100.0% men	1195	S: Employed, unemployed, not in workforce	S: T2D M: FPG, HbA1c	Unemployed men did not have higher risk for T2D (RR 0.43; 95% CI 0.08-2.32)) compared to employed men (adjusted for age, income, region of birth, marital status, smoking, BMI, waist, family history of diabetes, family history of obesity, high cholesterol, high BP). [d]	4.3% 4.3%	15.6% 15.6%
Müller et al. (2013a), Germany	Cross-sectional	45-74 y, 51.2% men	8871	S: Employed, unemployed, not in workforce (retired, other (vocational retraining, housewives, housemen))	S: T2D	Unemployed men (OR 0.91; 95% Cl 0.59-1.40) and women (OR 1.67; 95% CI 0.97-2.88) did not have higher risk for T2D compared to employed men and women (adjusted for age, social class, neighbourhood employment rate, marital status, body mass index, physical exercise and smoking status (only for men)).	18.8% 16.4% 21.9%	8.8% 10.0% 7.5%
Müller et al. (2013b), Germany [a]	Cross-sectional	45-74 y, 51.2% men	8879	S: Employed, unemployed, not in workforce (retired, other (vocational retraining, housewives, housemen)	S: T2D	Unemployed did not have higher risk for T2D (OR 1.12 95% CI 0.81-1.54) compared to employed (adjusted for neighbourhood unemployment rate and proportion of immigrants).	18.8% N/A N/A	8.8%
Poulsen at al. (2014), Denmark	Follow-up study (12 y)	30-59 y, 51.3% men	2,086,682	R: Employed (professionals; technicians and associate professionals; self-employed, non-	R: diagnosis of DM	DM incidence higher during the 12-year follow-up among unemployed (RR 2.13; 95%CI 2.06-2.21) compared to professional (adjusted for age, sex, country of origin and socio-economic status).	3.5% 2.9% 4.0%	5.8% 6.7% 4.9%

				classified, managers workers skilled at basic levels; workers in elementary occupations), unemployed, not in workforce (pensioners)				
Ramezankhani et al. (2014), Iran	Follow-up study (5 y)	≥ 20 y, 47.4% men	6647	S: Employed, unemployed, not in workforce (housewife, student, unemployed with income, other)	S: anti-diabetic medication M: FPG, OGTT	Incidence of T2D among unemployed 1.0%, employed 35.1%, housewife 50.5%, student 1.2%, unemployed with income 12.1%, other 0.1%. [d,e]	4.2% 4.1% 4.8%	11.0% 10.5% 11.4% 10.5%
Rautio et al. (2017), Finland	Cohort study, retro-spective follow-up (3 y)	~46 y, 43.6% men	4514	R: Employed, unemployed during the individually determined 3-year follow-up period preceding OGTT (≤1 year; >1 year)	M: OGTT	Men unemployed >1 year had higher risk for prediabetes (OR 1.61; 95%CI 1.03-2.51), and screen-detected T2D (OR 2.58; 95%CI 1.23-5.44) (adjusted for education, smoking, alcohol intake, physical activity and BMI). Corresponding figures for men unemployed ≤1 year were OR 1.26 (95%CI 0.88-1.82) and OR 1.12(95%CI 0.51-2.47). Among women unemployed > 1 year the figures not significant for prediabetes (OR 1.37; 95%CI 0.86-2.17) nor T2D (1.80; 95%CI 0.72-4.49). For women unemployed ≤1 year OR 1.30 (95%CI 0.85-1.97) and OR 2.02 (95%CI 0.88-4.64)	22.1% 23.2% 21.2%	3.0% 4.3% 2.0% 15.0%
Zhang et al. (2013), China	Cross-sectional	20-79 y, 48.6% men	7315	S: Employed (non-manual work, manual work), unemployed, not in workforce (retired)	R: T2D or medication M: FCPG, confirmed by measured FPG and 2-h PPPG	Unemployed did not have higher risk for T2D (OR 1.25, 95% CI 0.84-1.78) or IFG (OR 0.82, 95% CI 0.60-1.12) compared to manual work (adjusted for age, sex, BP, family history of diabetes, smoking, alcohol consumption, physical inactivity and BMI). [d]	24.4% 11.9% 36.8%	9.4% 8.3% 10.5% 7.3%

Abbreviations: T2D = type 2 diabetes, DM = diabetes mellitus, FCBG = fasting capillary blood glucose, CCBG = casual capillary blood glucose, FPG = fasting plasma glucose, IFG = impaired fasting glucose, FSG = fasting serum glucose, OGTT = oral glucose tolerance test, PPPG = postprandial plasma glucose, BMI = body mass index, BP = blood pressure, N/A = not applicable

[a] Not included in meta-analysis

[b] Additional data asked, not received from authors

[c] Error detected in the original Table III and corrected: In Table II the total number of individuals with IFG was given, but in Table III the same figure was told to cover IFG in the group unemployed and others only. When summing up the numbers in all groups in Table II, the plausible number of IFG in the group unemployed and others was calculated as 3, in accordance with the given percentage.
[d] Additional data asked and received from authors
[e] Error detected and corrected in the original Table 1 concerning number of unemployed persons with diabetes, persons without diabetes and total population. The corrected numbers were provided by the authors
[f] Unemployment rate is calculated as the percentage of unemployed persons of the total labor force, consisting of those in paid or self-employment plus the unemployed (OECD).
[g] Diabetes and prediabetes prevalence and incidence are calculated as the percentage of T2D patients of the total study population.

The association of unemployment with glucose metabolism: a systematic review and meta-analysis

International Journal of Public Health

Tuulia Varanka-Ruuska[1,2], Nina Rautio[1,3], Heli Lehtiniemi[1], Jouko Miettunen[1,4], Sirkka Keinänen-Kiukaanniemi[1,3,4,5], Sylvain Sebert[1,6,7], Leena Ala-Mursula[1]

[1] Center for Life Course Health Research, University of Oulu, Oulu, Finland
[2] Kallio Primary Health Care Unit, Ylivieska, Finland
[3] Unit of Primary Health Care, Oulu University Hospital, Oulu, Finland
[4] Medical Research Center Oulu, Oulu University Hospital and University of Oulu, Oulu, Finland
[5] Health Center of Oulu, Oulu, Finland
[6] Biocenter Oulu, University of Oulu, Oulu, Finland
[7] Department of Genomics of Complex Diseases, Imperial College, London, United Kingdom

Corresponding author: Tuulia Varanka-Ruuska , E-mail: tuulia.varanka-ruuska@oulu.fi

Appendix 1

Search strategy used in Scopus and Web of Science:

("glucose metabolism" OR "glucose tolerance" OR t2dm OR " type 2 diabet*" OR "type II diabet*" OR "diabetes mellitus type 2" OR "gestational diabetes" OR prediabete* OR niddm OR hyperglycem* OR "glucose intoler*" OR "glucose impairment") AND TOPIC: (employment OR unemployment OR jobless* OR "job loss")

Search strategy used in Medline Ovid:

1 exp Employment/
2 diabetes mellitus, type 2/ or diabetes, gestational/ or prediabetic state/ or hyperglycemia/ or glucose intolerance/
3 Blood Glucose/bl, me, ph [Blood, Metabolism, Physiology]
4 (glucose metabolism or glucose impairment).af.
5 1 and 2
6 1 and 3
7 1 and 4
8 5 or 6 or 7
9 exp Socioeconomic Factors/
10 2 or 3 or 4
11 9 and 10
12 *diabetes mellitus, type 2/ or *diabetes, gestational/ or *prediabetic state/ or *hyperglycemia/ or *glucose intolerance/
13 11 and 12
14 exp *Socioeconomic Factors/

15 13 and 14
16 *Blood Glucose/
17 14 and 16
18 4 and 9
19 work/ or return to work/ or work schedule tolerance/
20 2 and 19
21 3 and 19
22 4 and 19
23 20 or 21 or 22

Appendix 2

Quality assessment criteria and scoring for studies included in the systematic review

Criterion	Points	Study											
		Al-Baghli et al.	Azimi-Nezhad et al.	Bird et al.	Friedrich et al.	Kridli et al.	Martin et al.	Müller et al. (a)	Müller et al. (b)	Poulsen et al.	Ramezan khani et al.	Rautio et al.	Zhang et al.
1. Is the aim of the study clearly described?	Yes 1 No 0	1	1	1	1	1	1	1	1	1	1	1	1
2. Are the main outcomes to be measured clearly described in the methods section?	Yes 1 No 0	1	1	1	1	1	1	1	1	1	1	1	1
3. Are the characteristics of persons included in the study clearly described? [a]	Yes 1 No 0	1	1	1	1	1	1	1	1	1	1	1	1
4. Are the distributions of principal confounders in each group of subjects to be compared provided and clearly described? [a]	Yes 2 Partially 1 No 0	2	2	2	2	2[b]	2[a]	1	1	2	1[c]	2	1
5. Are the main findings of the study clearly described?	Yes 1 No 0	1	1	1	1	1	1	1	1	1	1	1	1
6. Does the study provide estimates of the random variability in the data for the main outcome?	Yes 1 No 0	1	1	1	1	1	1	1	1	1	1	1	1
7. Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where the probability is less than 0.001?	Yes 1 No 0	1	0	1	0	0	0	0	0	0	0	1	0
8. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	Yes 1 No 0 Unable to determine 0	0	1	1	1	0	1	1	1	1	1	1	1

9. Were the subjects participating the study representative of the entire population? (The participation rates and the distributions of the confounders in the study population and the source population given) [a]	Yes 1 No 0 Unable to determine 0	0	0	1	0	0	1	0	0	1	0	0	1
10. If any of the results of the study were based on data dredging was this made clear?	Yes 1 No 0 Unable to determine 0	1	1	1	1	1	1	1	1	1	1	1	1
11. Were the statistical test used to assess the main outcomes appropriate?	Yes 1 No 0 Unable to determine 0	1	1	1	1	1	1	1	1	1	1	1	1
12. Were the main outcome measures used accurate (valid and reliable)?	Yes 1 No 0 Unable to determine 0	1	0	1	1	1	1	1	1	1	1	1	1
Total	Max 13	11	10	13	11	10	11	10	10	12	10	12	11

[a]Data in the article or in the article authors refer to
[b]No confounders used
[c]Decision tree, no confounders used