



## **Study of glucose homeostasis in burnout cases using an oral glucose tolerance test**

Downloaded from: <https://research.chalmers.se>, 2025-01-19 22:39 UTC

Citation for the original published paper (version of record):

Lennartsson, A., Jonsdottir, I., Jansson, P. et al (2025). Study of glucose homeostasis in burnout cases using an oral glucose tolerance test. *Stress: the International Journal on Biology of Stress*, 28(1). <http://dx.doi.org/10.1080/10253890.2024.2438699>

N.B. When citing this work, cite the original published paper.

# Study of glucose homeostasis in burnout cases using an oral glucose tolerance test

Anna-Karin Lennartsson, Ingibjörg H. Jonsdottir, Per-Anders Jansson & Anna Sjörs Dahlman

To cite this article: Anna-Karin Lennartsson, Ingibjörg H. Jonsdottir, Per-Anders Jansson & Anna Sjörs Dahlman (2025) Study of glucose homeostasis in burnout cases using an oral glucose tolerance test, *Stress*, 28:1, 2438699, DOI: [10.1080/10253890.2024.2438699](https://doi.org/10.1080/10253890.2024.2438699)

To link to this article: <https://doi.org/10.1080/10253890.2024.2438699>



© 2024 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group



Published online: 17 Dec 2024.



Submit your article to this journal [↗](#)



Article views: 482



View related articles [↗](#)



View Crossmark data [↗](#)

RESEARCH ARTICLE



## Study of glucose homeostasis in burnout cases using an oral glucose tolerance test

Anna-Karin Lennartsson<sup>a,b</sup>, Ingibjörg H. Jonsdottir<sup>a,b</sup>, Per-Anders Jansson<sup>c</sup> and Anna Sjörs Dahlman<sup>d,e</sup>

<sup>a</sup>The Institute of Stress Medicine, Region Västra Götaland, Gothenburg, Sweden; <sup>b</sup>School of Public Health and Community Medicine, Institute of Medicine, Sahlgrenska Academy at the University of Gothenburg, Gothenburg, Sweden; <sup>c</sup>Wallenberg Laboratory, Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; <sup>d</sup>Swedish National Road and Transport Research Institute (VTI), Linköping, Sweden; <sup>e</sup>Department of Electrical Engineering, and SAFER Vehicle and Traffic Safety Centre, Chalmers University of Technology, Gothenburg, Sweden

### ABSTRACT

Burnout is caused by long term psychosocial stress and has, besides the fatigue and mental health burden, been associated with increased risk of adverse physical health, such as for example type 2 diabetes. This study aims to investigate the glucose and insulin levels in individuals with stress related burnout, by assessing these metabolic markers in response to a standard oral glucose tolerance test (OGTT). 38 cases with burnout (13 men and 25 women) and 35 healthy controls (13 men and 22 women) in the age 24–55 were included in the study. The burnout group overall did not differ from healthy controls in glucose or insulin levels during the OGTT. However, the burnout cases who reported more severe burnout symptoms exhibited significantly higher levels of both glucose and insulin levels during the OGTT compared to burnout cases reporting lower severity of symptoms. Furthermore, the group of burnout cases who reported symptoms of depression exhibited higher insulin levels during OGTT compared to the burnout cases without depressive symptoms. The observed higher levels in the burnout cases with most severe symptoms indicate an increased diabetic risk in these patients and it may be of importance to follow glucose and insulin levels in individuals with more severe symptoms of burnout i.e. to perform an OGTT.

### ARTICLE HISTORY

Received 5 June 2024

Accepted 23 November 2024

### KEYWORDS

Burnout; depression; glucose; insulin; oral glucose tolerance test; insulin resistance

### Introduction

Burnout has been defined as a negative affective state consisting of emotional exhaustion, cognitive weariness and physical fatigue which is caused by chronic psychosocial stress (Melamed et al., 1992). Burnout is often accompanied with symptoms of depression and anxiety. Besides the fatigue and mental health burden, burnout is associated with increased risk of adverse physical health (Honkonen et al., 2006; Lerman et al., 1999; Melamed et al., 1992; Melamed, Berliner, 2006; Melamed, Shapira, 2006; Sheiner et al., 2002; Toker et al., 2005). For example, burnout has been associated with increased risk of developing type 2 diabetes (Melamed, Berliner, 2006; Melamed, Shapira, 2006). It has been suggested that psychosocial stress, by neuroendocrine pathways, induce insulin resistance (Björntorp et al., 1999; Rosmond, 2003; Rosmond & Björntorp, 2000), a pre-diabetic state which implicates reduced capacity to transport glucose into cells (and thus reduced capacity to utilize glucose as energy source). To compensate for this, the beta-cells of pancreas produce more insulin which eventually could result in, if maintained, chronic hyperglycemia and type 2 diabetes (Tabák et al., 2012).

The present study aims to investigate the glucose and insulin levels in individuals with stress related burnout, by assessing these metabolic markers in response to a standard oral glucose tolerance test (OGTT). In a previous study from our research group, Sjörs et al. (2013) investigated fasting levels of insulin and glucose in 90 patients with stress related clinical burnout (and 90 controls) and found higher levels of insulin in the patients compared to the healthy controls. The indexes HOMA-IR and HOMA- $\beta$ , which mirror insulin resistance and  $\beta$ -cell function, were both significantly higher in the patients than controls. We also found slightly lower, but statistically significant, fasting glucose levels, but no difference in HbA1c, between patients with stress related clinical burnout and controls. There are only few studies performed investigating glucose and insulin levels in relation to stress related burnout, and the existing studies do not show consistent results (Deneva et al., 2019; Grossi et al., 2003; Sjörs et al., 2013). In the present study, we aim to further investigate the circulating glucose and insulin concentrations in burnout subjects, conducting an oral glucose tolerance test. As far as we know, OGTT has previously not been used in studies on burnout subjects. OGTT detects pre-diabetic stages more sensitive than a single fasting glucose or HbA1c. While

**CONTACT** Anna-Karin Lennartsson  [karin.lennartsson@vregion.se](mailto:karin.lennartsson@vregion.se)  Carl Skottsbergs gata 22B, 413 19 Göteborg, Sweden.

© 2024 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The terms on which this article has been published allow the posting of the Accepted Manuscript in a repository by the author(s) or with their consent.

a single glucose measurement only can define impaired fasting glucose (IFG), OGTT mirror the patient's ability to normalize the glucose levels after glucose intake, thus it detects impaired glucose tolerance (IGT). Furthermore, OGTT offers the opportunity to study insulin resistance and beta-cell function, by HOMA indexes, using fasting levels of glucose and insulin. Thus, the primary aim was to investigate if fasting level of glucose and HbA1c as well as insulin resistance (HOMA-IR) and glucose tolerance differ between burnout cases and healthy controls. A secondary aim was to investigate if severity of mental health symptoms (burnout, depression and anxiety) among the burnout cases is associated with fasting glucose, HOMA-IR, HbA1c or glucose tolerance.

## Method

### Participants

38 individuals with burnout (13 men and 25 women) and 35 healthy controls (13 men and 22 women) in the age 24–55 were included in the study. The burnout cases were recruited via advertisements in waiting rooms at occupational and primary care units in Gothenburg, Sweden. Inclusion criteria for burnout cases were a mean score  $\geq 4.4$  on the Shirom–Melamed Burnout Questionnaire (SMBQ) and self-rated symptoms for severe exhaustion disorder assessed with the self-rated exhaustion disorder (s-ED) questionnaire. A mean SMBQ score above 4.4 has previously been shown to discriminate patients with clinical burnout from healthy controls (Lundgren-Nilsson et al., 2012). The s-ED questionnaire is based on the Swedish diagnostic criteria for Exhaustion Disorder, which is the diagnosis used for clinical burnout in Sweden (Glise et al., 2014). Self-rated depression and anxiety was also allowed in the patient group. Healthy controls were recruited among volunteers that had previously responded to advertisements about participation in different studies at the Institute of Stress Medicine in Gothenburg, Sweden. The age of the participants in the control group was 20–61 years and they were recruited to match the mean age in the patient group. Before inclusion, the subjects underwent a screening test, including questionnaires, anthropometric measurements and blood sampling. P-glucose, HbA1c, Hb, TSH, T4 and homocysteine were assessed in the blood samples. The screening was performed to ensure the following exclusion criteria: having a body mass index less than  $18.5 \text{ kg/m}^2$  or higher than  $30 \text{ kg/m}^2$ , high blood pressure, infection, anemia, vitamin B12 deficiency (high homocysteine), known systemic disease such as diabetes or thyroid disease, known psychiatric disease (except self-rated stress-related exhaustion, depression and anxiety in the burnout cases group), alcohol abuse, pregnancy, breast feeding, menopause or use of drugs with systemic effects, including oral contraceptives but excluding antidepressants for the burnout cases. All participants gave written informed consent before entering the study and were informed that they could withdraw their participation at any time. The study was conducted according to the Declaration of Helsinki and approved by the Regional Ethical Board, Gothenburg, Sweden, Dnr 755-15.

### Oral glucose tolerance test (OGTT)

All participants underwent an OGTT performed according to the World Health Organization (WHO) criteria 1985. A venous catheter was inserted to enable blood sampling at regular intervals and during the test study participants rested sitting in an armchair reading or listening to the radio. Before the glucose load, the first blood samples were taken, constituting the fasting samples. The subjects then received 200 ml of glucose solution (75 g of glucose) and blood samples were drawn 30, 60, 90 and 120 min after the glucose load. Total blood loss was about 110 ml. Blood samples for analysis of plasma glucose and serum insulin were sent directly to the Laboratory for Clinical Chemistry at Sahlgrenska University Hospital for analysis.

### Glucose and insulin measures

2-h venous plasma glucose value  $\geq 11.1 \text{ mmol/L}$  was classified as diabetes and  $7.8\text{--}11.0 \text{ mmol/L}$  was classified as impaired glucose tolerance (IGT). Insulin resistance and  $\beta$ -cell function was calculated according to the homeostasis model assessment (HOMA) (Matthews et al., 1985). HOMA-IR (insulin resistance) was calculated as  $(\text{fasting glucose} \times \text{insulin})/22.5$  and HOMA- $\beta$  was calculated according to the formula  $(20 \times \text{insulin})/(\text{glucose}-3.5)$ .

### Questionnaires

The participants answered several questionnaires assessing perceived stress and symptoms of burnout, anxiety and depression. They also answered questionnaires regarding their physical activity level. Perceived stress was assessed with the Perceived Stress Scale (PSS-14) (Cohen et al., 1983). This includes 14 questions capturing perceived stress during the previous month in different ways. The Shirom–Melamed Burnout Questionnaire (SMBQ) (Melamed et al., 1992) was used to measure severity of burnout symptoms. SMBQ contains 22 items (graded 1–7) measuring the different aspects of burnout: emotional and physical exhaustion, tension, listlessness and cognitive weariness. A mean burnout index was calculated for each participant. The index ranges from 1 to 7 (no to high burnout symptom load). The Hospital Anxiety and Depression (HAD) scale was used to assess self-reported symptoms of depression and anxiety (Bjelland et al., 2002; Zigmond & Snaith, 1983). HAD contains 14 items (7 items for each subscale). The scores for each subscale were used to classify “non-cases” (0–7), “possible cases” (8–10), and “cases” (above 10) of anxiety and depression, respectively. Participants reported their physical activity level (the past year) with the Saltin–Grimby Physical Activity Level Scale (Saltin & Grimby, 1968). This scale is a single-item question with four response options. The first level corresponds to a sedentary lifestyle, while levels 2–4 represent graded increases in activity level from light to strenuous exercise training.

## Statistical analysis

Kolmogorov–Smirnov test was used for each study variable to test whether data were normally distributed. The variables which showed a non-normal distribution underwent logarithmic transformation. After logarithmic transformation (ln), the Kolmogorov–Smirnov test was used again to control whether the new variable showed a normal distribution. The distribution of men and women and the distribution of sedentary/physical activity individuals in the two groups (cases and controls) was compared using Chi-square test. *T* test was used to compare age, BMI and WHR between the groups. The analyses on BMI and WHR were also performed separately in men and women. Mann–Whitney *U* test was used to compare scores for perceived stress, burnout and anxiety between cases and controls. The frequencies of usage of antidepressant medication among the different subgroups of burnout cases were produced. Levels of HbA1c and fasting glucose (measured at screening) were compared between burnout cases and controls using *t* test. To investigate possible differences between burnout cases and controls in response to OGTT, mixed between and within analysis of variance (ANOVA) including interaction was computed with hormonal level (insulin and glucose, respectively) at the six different time points as the within variable and Group (cases vs. controls) as the between variable. Log values of glucose and insulin was used. The 2-h glucose value (log values), HOMA-IR and HOMA- $\beta$  were compared between burnout cases and controls using *t* tests. To investigate whether glucose and insulin measures could be related to severity of symptoms in the burnout cases, Spearman's rank correlation test was performed between scores of depression, anxiety and burnout on one hand and the different insulin and glucose levels/measures on the other hand. To further

investigate whether insulin and glucose measures were associated with severity of burnout, the burnout cases were divided into three groups (tertiles) based on their burnout scores. Mixed between/within ANOVAs was used to compare the response of glucose and insulin, respectively, between the group of burnout cases with most severe burnout symptoms and the others. Log values of glucose and insulin was used. *T* test was used to compare the 2-h glucose (log), HbA1c and HOMA-IR between the subjects with the most severe burnout symptoms and those with less severe symptoms. Further, the concentrations of glucose and insulin during OGTT was compared between the non-depressed burnout cases (HAD-D 0–10) and the depressed burnout cases (HAD-D > 10) using mixed between/within ANOVA. Log values of glucose and insulin were used. The 2-h glucose levels (log), HbA1c and HOMA-IR was compared between depressed and non-depressed using *t* test. The same analyses which were performed for the HAD Depression scale was performed with the HAD Anxiety scale, thus comparisons made between the group with anxiety (>10) and the other burnout cases with regards to insulin and glucose response to OGTT and HbA1c, HOMA-IR and the 2-h glucose measure. Analyses were conducted with IBM SPSS Statistics 29 (IBM Armonk, NY, USA).

## Results

### Background characteristics

The study sample included 38 burnout cases (66% women) and 35 healthy controls (63% women). The background characteristics for the burnout cases and controls are reported in Table 1. There were no differences between the groups regarding age, BMI, WHR or tobacco use. As expected, the

**Table 1.** Background characteristics in burnout cases ( $n=38$ ) and controls ( $n=35$ ).

	Burnout cases		Controls		<i>p</i> value
	Mean (range)	<i>n</i> (%)	Mean (range)	<i>n</i> (%)	
Age, years	42 (26–55)		42 (24–61)		0.855
Sex (% women)	66%		63%		0.812
BMI, kg/m <sup>2</sup>	22.6 (16.6–30.4)		23.8 (18.7–29.4)		0.090
Men separately	24.3 (21.7–30.4)		25.0 (20.4–29.4)		0.484
Women separately	21.7 (16.6–28.2)		23.1 (18.7–28.9)		0.120
WHR	0.82 (0.70–0.95)		0.84 (0.71–1.07)		0.326
Men separately	0.88 (0.78–0.95)		0.91 (0.84–1.07)		0.204
Women separately	0.79 (0.70–0.93)		0.80 (0.71–0.88)		0.738
Tobacco user (snuffing or smoking)		3 (8%)		6 (17%)	0.390
Antidepressant use		11 (29%)		0 (0%)	
Perceived stress (PSS-14)	33 (17–50)		16 (3–36)		<0.001
Depression (HAD)	8 (2–17)		2 (0–6)		<0.001
<7		14 (37%)			
7–10		18 (47%)			
>10		6 (16%)			
Anxiety score (HAD)		11 (1–18)	4 (1–10)		<0.001
<7		5 (13%)			
7–10		14 (37%)			
>10		19 (50%)			
Burnout score (SMBQ)	5.24 (4.00–6.83)		1.99 (1.17–2.72)		<0.001
Lower tertile 4.00–4.89		12 (31.6%)			
Middle tertile 5.17–5.72		15 (39.5%)			
Upper tertile 5.78–6.83		11 (28.9%)			
Physical activity level					0.026
Sedentary		11 (29%)		1 (3%)	
Light physical activity		13 (34%)		15 (43%)	
Moderate physical activity		13 (34%)		17 (49%)	
Hard training or competitive sports		1 (3%)		2 (6%)	

BMI, Body Mass Index; WHR, Waist Hip Ratio; PSS-14, Perceived Stress Scale with 14 questions; HAD, Hospital Anxiety Depression Scale; SMBQ, Shirom–Melamed Burnout Questionnaire.

burnout group reported significantly higher perceived stress scores as well as symptoms of depression, anxiety and fatigue compared to controls. The burnout group was sedentary to a higher extent than the control group. Eleven of the 38 burnout cases (29%) in the present study were on antidepressant medication (Escitalopram, Sertraline, Mirtazapine, Citalopram, or Vortioxetine). The usage of antidepressant medication was same in the group of burnout cases with the most severe symptoms (highest tertile on SMBQ) as in those reporting less severe symptoms (27% compared to 29%, respectively).

### Glucose and insulin in burnout cases and controls

There was no overall difference between burnout cases and controls with regard to HbA1c (mmol/mol) (32 and 31, respectively,  $p = 0.500$ ) or fasting glucose (mmol/L) levels (5.29 and 5.31, respectively,  $p = 0.816$ ). Glucose and insulin levels in burnout cases and controls during the OGTT are reported in Figure 1. Repeated measures ANOVA showed, as expected, a significant effect of time on both glucose ( $F = 76,158$ ,  $p < 0.001$ ) and insulin ( $F = 335.44$ ,  $p < 0.001$ ). There was no interaction effect between time and group, thus there were similar response patterns in burnout cases and controls with regard to glucose ( $p = 0.306$ ) and insulin ( $p = 0.681$ ). There were no effects of group, thus no difference with regard to glucose ( $p = 0.805$ ) or insulin levels ( $p = 0.435$ ) between the burnout cases and controls during the OGTT. The 2 hours glucose value is the measurement used to investigate whether the study subject has a normal glucose tolerance ( $< 7.8$  mmol/L), impaired glucose tolerance (7.8–11.0 mmol/L) or diabetes ( $\geq 11.1$  mmol/L). Sixty-nine of 73 the study participants (94.5%) exhibited normal glucose tolerance. Two controls and one burnout subject exhibited impaired glucose tolerance and one individual in the burnout case group fulfilled type 2 diabetes criteria. There was no significant difference between burnout cases and controls with regard to the level of glucose at the 2 h measurement of the OGTT (5.56 and 5.24 mmol/L, respectively,  $p = 0.321$ ).

Further, no significant differences were seen between burnout cases and controls regarding insulin resistance and beta cell function indicated by the indexes HOMA-IR (1.40 and 1.57, respectively,  $p = 0.592$ ) and HOMA- $\beta$  (70.8 and 76.3, respectively,  $p = 0.945$ ). Thus, in general, no differences in glucose homeostasis were seen between burnout subjects and controls.

### Symptoms of burnout is associated with glucose and insulin levels during OGTT

Burnout score did not correlate significantly with level of fasting glucose ( $p = 0.268$ ), 2-h glucose ( $p = 0.128$ ), fasting insulin ( $p = 0.139$ ), HOMA-IR ( $p = 0.118$ ) or HbA1c ( $p = 0.148$ ). However, burnout scores were positively correlated with insulin levels at the time point 60 minutes into the test ( $r = 0.351$ ,  $p = 0.031$ ) and glucose level 90 minutes into the test ( $r = 0.356$ ,  $p = 0.028$ ). To further investigate whether insulin and glucose level were associated with degree of burnout symptoms, the burnout cases were divided into three groups (tertiles) based on their burnout scores. Insulin and glucose levels during the OGTT were then compared between the burnout groups using mixed between-within ANOVAs. Figure 2 shows the glucose and insulin levels during the OGTT in the three burnout score groups. The group of burnout cases with the most severe burnout symptoms (mean SMBQ scores 5.78–6.83) exhibited significantly higher levels of glucose ( $F = 11.510$ ,  $p = 0.002$ ) and insulin ( $F = 7.299$ ,  $p = 0.0011$ ) during the OGTT compared to the others. No difference in HbA1c ( $p = 0.244$ ) or the 2-h glucose ( $p = 0.175$ ) were seen between the burnout cases with more severe symptoms and the others. Figure 3 report HOMA-IR in the three burnout groups. HOMA-IR was significantly higher in the burnout cases with severe burnout symptoms compared to the others ( $t = -2.247$ ,  $p = 0.031$ ). There were no differences between the two groups with lower burnout scores with regard to HOMA-IR or levels of glucose and insulin during the OGTT (data not shown).

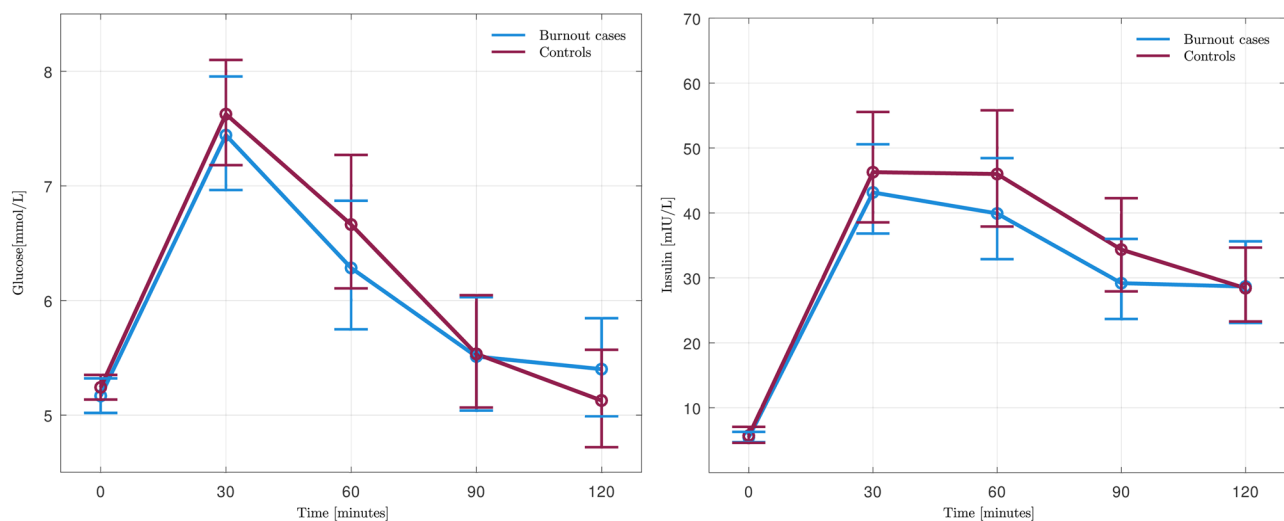
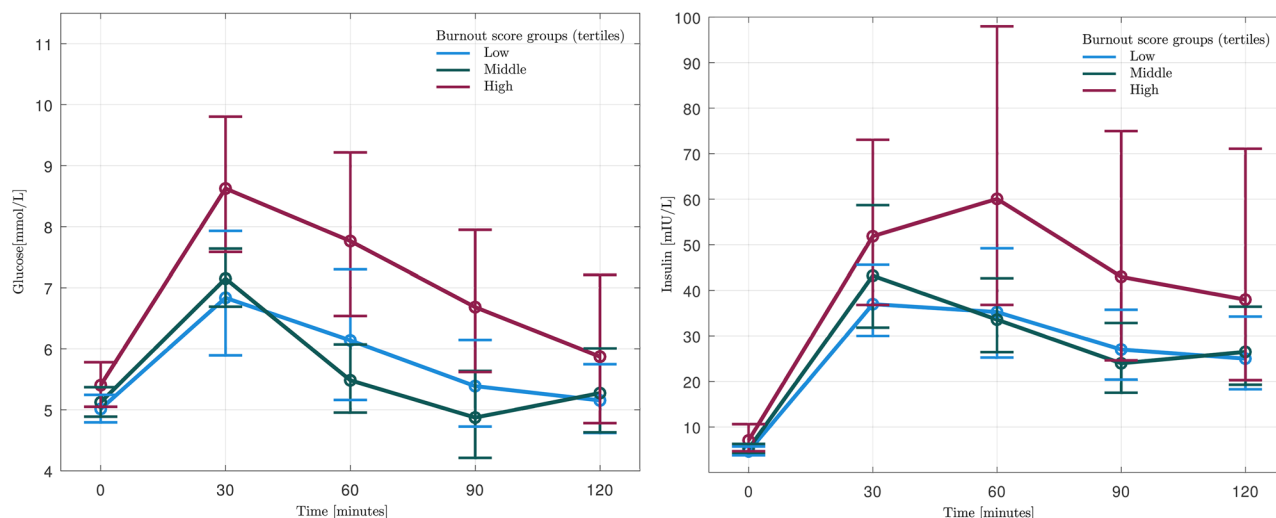
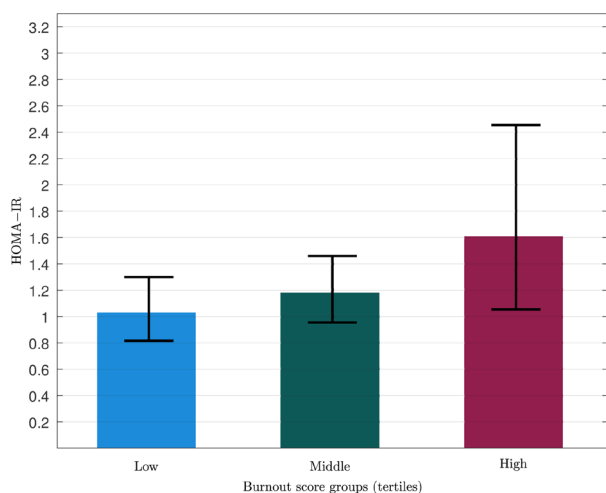


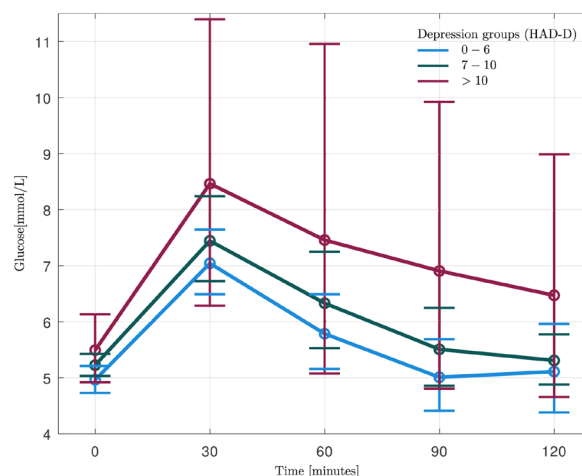
Figure 1. Glucose and insulin levels (means and 95% CI) in burnout cases ( $n=38$ ) and controls ( $n=35$ ) during OGTT.



**Figure 2.** Glucose and insulin levels (means, 95% CI) during OGTT in burnout cases with different burnout scores (Low,  $n = 12$ ; Middle,  $n = 15$ ; High,  $n = 11$ ).



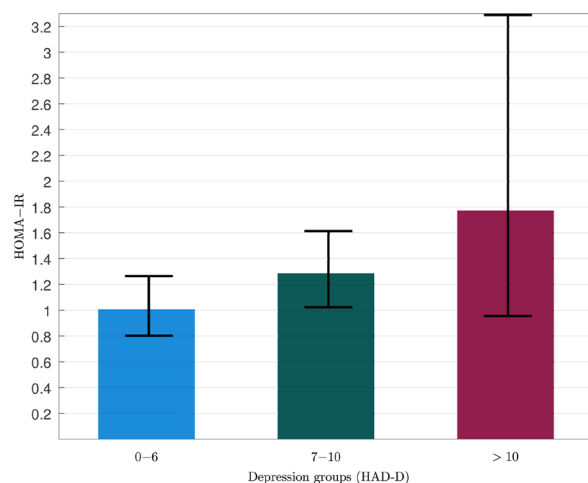
**Figure 3.** HOMA-IR (mean, 95% CI) during OGTT in burnout cases with different burnout scores (Low,  $n = 12$ ; Middle,  $n = 15$ ; High,  $n = 11$ ).



**Figure 4.** Glucose levels (95% CI) during the OGTT in burnout cases scoring high depression (HAD-D  $>10$ ,  $n = 6$ ), moderate depression (HAD-D 7-10,  $n = 18$ ) and no depression (HAD-D 0-6,  $n = 14$ ).

### **Symptoms of depression but not symptoms of anxiety were associated with glucose and insulin levels during OGTT**

There were positive correlations between depression scores and fasting glucose level ( $r = 0.343$ ,  $p = 0.035$ ), the 2-h glucose level ( $r = 0.332$ ,  $p = 0.041$ ), fasting insulin ( $r = 0.322$ ,  $p = 0.049$ ) and HOMA-IR ( $r = 0.356$ ,  $p = 0.028$ ). HbA1c was not correlated with depression score ( $p = 0.936$ ). The patients were divided into three groups based on their depression score. The glucose levels during OGTT in these groups are reported in Figure 4. The concentrations of glucose during OGTT were compared between the non-depressed burnout cases (0-10) and depressed burnout cases ( $>10$ ) using mixed between-within ANOVA. Glucose levels during the OGTT were significantly higher among the depressed burnout cases than the non-depressed burnout cases ( $F = 5.954$ ,  $p = 0.020$ ). The 2-h glucose and HOMA-IR differed significantly between the depressed and non-depressed burnout cases ( $t = -2.093$ ,  $p = 0.043$  and  $t = -2.069$ ,  $p = 0.046$ , respectively), but no difference in HbA1c was seen ( $p = 0.815$ ). Figure 5 reports the HOMA-IR in the depression groups. There was no difference



**Figure 5.** Mean HOMA-IR (95% CI) in burnout cases scoring high depression (HAD-D  $>10$ ,  $n = 6$ ), moderate depression (HAD-D 7-10,  $n = 18$ ) and no depression (HAD-D 0-6,  $n = 14$ ).

between depressed and non-depressed burnout cases in insulin levels during OGTT (data not shown). Anxiety scores did not correlate with any of the glucose or insulin measures

and mixed between-within ANOVA did not show any differences between the groups with different anxiety scores (0–6, 7–10, >10) (data not shown).

## Discussion

### *Main results*

This study investigated circulating glucose and insulin concentrations in individuals with burnout using a standard OGTT, and to our knowledge this is the first study measuring OGTT in burnout subject. The main results are that the burnout group overall did not differ from healthy controls. However, the burnout subjects who reported more severe burnout symptoms exhibited significantly higher levels of both glucose and insulin levels during the OGTT compared to those reporting lower severity of symptoms. Furthermore, the group of burnout cases who scored higher level of symptoms of depression exhibited higher insulin levels during OGTT compared to those without depressive symptoms. The observed higher levels indicate a diabetic risk in these burnout cases.

### *Comparisons to previous research*

As previously mentioned, Melamed et al. (Melamed et al., 2006) found that burnout was associated with increased risk of diabetes. They prospectively studied 677 apparently healthy working men and women (for 3–5 years) and found an association with burnout, with a 1.84-fold increase in risk of developing type 2 diabetes, even after controlling for several potential confounding variables. Further, a recently published systematic review and meta-analysis by Strikwerda et al. (Strikwerda et al., 2021) observed a 1.8 times higher odds of prevalent type 2 diabetes in individuals with burnout and vital exhaustion compared to those without. However, they found lack of significant associations between burnout/vital exhaustion and markers of glycemic control. There are few studies which investigated the possible links between burnout and circulating glucose and insulin levels, and the existing studies show conflicting results. Grossi et al. (Grossi et al., 2003) investigated physiological correlates of burnout in women and found that HbA1c levels were higher in the participants with high compared to low burnout scores measured with SMBQ while fasting glucose or insulin were not assessed in this study. In the present investigation, no overall differences were seen in HbA1c levels between burnout cases and controls. Further, no difference in HbA1c was seen between the burnout cases with more severe symptoms and the others. Bellingrath et al. (2009) studied measures of the allostatic load concept in relation to burnout measures in 104 healthy female schoolteachers, 25–60 years old. They found no correlation between fasting glucose and HbA1c on one hand and measures of burnout (Vital exhaustion, Maslach Burnout inventory) on the other hand. Deneva et al. (2019) studied insulin and glucose levels among other biological markers in 93 physicians with burnout, according to their ratings on Maslach Burnout inventory (MBI) scale, compared to 230 subjects without burnout, and found that cortisol, ACTH, fasting glucose

and HbA1c, but not insulin, were significantly higher in the burnout subjects. As mentioned in the introduction, a previous study from our research group, Sjörs et al. (2013), investigated fasting levels of insulin and glucose in 90 patients with stress related clinical burnout (and 90 controls) and found higher levels of insulin in the patients compared to the healthy controls. The indexes HOMA-IR and HOMA- $\beta$ , which mirror insulin resistance and  $\beta$ -cell function, respectively, were also shown to be significantly higher in the patients compared to control controls (Sjörs et al., 2013). In the present study we did not find any difference between patients and controls. However, we found that the patients with severe burnout symptoms exhibited levels indicating a prediabetic state, thus high levels of glucose and insulin during the OGTT and higher HOMA-IR. Equivalent comparisons between groups with different severity of symptoms were not performed in our previous study. We also found that the burnout cases who reported symptoms of depression exhibited higher insulin levels during OGTT and higher HOMA-IR compared to the others. The subjects in our previous study were a more selected group of clinical patients admitted to an outpatient clinic specializing in stress-related illness. The burnout subjects in the present study had less severe stress-related exhaustion but most probably they better represent individuals seeking care for stress-related problems in general. Depression has previously been linked to insulin resistance (Leonard & Wegener, 2020; Macchi et al., 2020) and increased risk for types 2 diabetes (Eaton et al., 1996), and the link is suggested to be elevated cortisol levels, among other mechanisms.

### *Antidepressant medication and its effects on the results*

The research on the effects of antidepressants on insulin sensitivity and glucose metabolism show diverse results. The most studied group among the antidepressant pharmacological agents is the selective serotonin reuptake inhibitors (SSRI). Some SSRI have in some studies been shown to have a positive effect on insulin sensitivity and glucose homeostasis (Buhl et al., 2010; McIntyre et al., 2006; Weber-Hamann et al., 2006), while other SSRI antidepressants seem to negatively influence insulin resistance (Brown et al., 2008; Kesim et al., 2011; Kivimäki et al., 2010). However, results are incongruent, even among studies on the same sort of SSRI. The usage of antidepressant medication was similar in the group of burnout cases with the most severe symptoms and the others and none of the burnout cases who scored depression was on antidepressant medication. We also performed post hoc analyses showing no difference in any of the glucose or insulin measures between the antidepressant users and the other burnout cases (data not shown). A cautious conclusion it that use of antidepressants is not the main driver for the impaired insulin resistance and glucose homeostasis seen in the group of burnout cases with more severe symptoms.

### *Methodological considerations*

Several methodological considerations should be mentioned. This is a relatively small study, which becomes even more evident when the group of burnout cases is divided into three



different subgroups. One reflection is that the difference seen in this study between high and low symptoms seem to be clear even in such a small sample. A limitation of the study is that the small sample size restricted us from controlling for background factors such as for example age, BMI and sex. However, there was no difference between groups, or sub-groups (data not shown) in any of the background variables which most probably makes this of minor importance. Since 3 patients and 6 controls were tobacco users it should be mentioned that smoking and snuff (Carlsson et al., 2017; Persson et al., 2000) may increase the risk of type 2 diabetes and thus may influence the results. However, post hoc analysis was performed showing that there was no difference in any of the glycemic measures between tobacco users and the others (data not shown).

It should be noted that, since the study is cross-sectional, it is not possible to determine the causality between burnout and glucose homeostasis. Further, only self-reports are used in this study, thus the burnout case population has not been clinically assessed for any diagnoses. However, the assessment tools used have been validated to be useful in separating clinical population from a nonclinical population. The cross-sectional design of the study does not allow investigation of the causal link between burnout and glycemic control.

## Conclusions

Burnout subjects in general do not exhibit different glucose and insulin levels during OGTT compared to healthy controls. However, the results indicate that the group of burnout cases who suffer from severe exhaustion and/or depression exhibit glucose and insulin levels indicating an increased diabetic risk. Thus, in clinical practice, the patients with burnout should be examined with regards to glucose and insulin, to detect prediabetes on an early stage. The results should be confirmed by other studies. Further studies could also explore the possible mechanisms between insulin resistance and symptoms of fatigue/depression.

## Disclosure of interest

The authors report no conflict of interest.

## Funding

This work was supported by a grant from the Swedish Research Council for Health, Working Life and Welfare (FORTE) [grant number 2013-1123].

## Notes on contributors

**Anna-Karin Lennartsson**, MD, PhD, is affiliated researcher at the Institute of Stress Medicine and the Institute of Medicine at Gothenburg University, Sweden. Her research interest is stress physiology, with focus mainly on stress endocrinology.

**Ingibjörg H. Jonsdottir** is a Professor in Public health science at the School of Public Health and Community Medicine, Gothenburg University and a director for the Institute of Stress Medicine, Region Västra Götaland. Her research interest covers different aspects of stress research including promotive, preventive, and therapeutic perspective as well as the underlying biological mechanisms of stress-related mental health problems.

**Per-Anders Jansson**, MD, PhD, is a Professor at the Institute of Medicine, Sahlgrenska Academy, Gothenburg University, Sweden. His research interest is mechanisms behind insulin resistance in prediabetes/type 2 diabetes. The overall aim of his work is to elucidate the metabolic impact of insulin-resistance and to implement novel strategies to prevent and treat type 2 diabetes.

**Anna Sjörs Dahlman**, PhD, is a senior researcher at the Swedish National Road and Transport Research Institute and an Adjunct Associate Professor with the Department of Biomedical Signals and Systems, Chalmers University of Technology, Sweden. Her research interests include occupational health, stress-related illness, professional drivers' health and fitness-to-drive.

## Data availability statement

The data used in this study is available from the corresponding author upon request.

## References

- Bellingrath, S., Weigl, T., & Kudielka, B. M. (2009). Chronic work stress and exhaustion is associated with higher allostatic load in female school teachers. *Stress (Amsterdam, Netherlands)*, 12(1), 37–48. <https://doi.org/10.1080/10253890802042041>
- Bjelland, I., Dahl, A. A., Haug, T. T., & Neckelmann, D. (2002). The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *Journal of Psychosomatic Research*, 52(2), 69–77. [https://doi.org/10.1016/s0022-3999\(01\)00296-3](https://doi.org/10.1016/s0022-3999(01)00296-3)
- Björntorp, P., Holm, G., & Rosmond, R. (1999). Hypothalamic arousal, insulin resistance and type 2 diabetes mellitus. *Diabetic Medicine: A Journal of the British Diabetic Association*, 16(5), 373–383. <https://doi.org/10.1046/j.1464-5491.1999.00067.x>
- Brown, L. C., Majumdar, S. R., & Johnson, J. A. (2008). Type of antidepressant therapy and risk of type 2 diabetes in people with depression. *Diabetes Research & Clinical Practice*, 79(1), 61–67. <https://doi.org/10.1016/j.diabres.2007.07.009>
- Buhl, E. S., Jensen, T. K., Jessen, N., Elfving, B., Buhl, C. S., Kristiansen, S. B., Pold, R., Solskov, L., Schmitz, O., Wegener, G., Lund, S., & Petersen, K. F. (2010). Treatment with an SSRI antidepressant restores hippocampo–hypothalamic corticosteroid feedback and reverses insulin resistance in low-birth-weight rats. *American Journal of Physiology, Endocrinology & Metabolism*, 298(5), E920–9. <https://doi.org/10.1152/ajpendo.00606.2009>
- Carlsson, S., Andersson, T., Araghi, M., Galanti, R., Lager, A., Lundberg, M., Nilsson, P., Norberg, M., Pedersen, N. L., Trolle-Lagerros, Y., & Magnusson, C. (2017). Smokeless tobacco (snus) is associated with an increased risk of type 2 diabetes: Results from five pooled cohorts. *Journal of Internal Medicine*, 281(4), 398–406. <https://doi.org/10.1111/joim.12592>
- Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of perceived stress. *Journal of Health & Social Behavior*, 24(4), 385–396. <https://doi.org/10.2307/2136404>
- Deneva, T., Ianakiev, Y., & Keskinova, D. (2019). Burnout syndrome in physicians—psychological assessment and biomarker research. *Medicina (Kaunas, Lithuania)*, 55(5), 209. <https://doi.org/10.3390/medicina55050209>
- Eaton, W. W., Armenian, H., Gallo, J., Pratt, L., & Ford, D. E. (1996). Depression and risk for onset of type II diabetes. A prospective population-based study. *Diabetes Care*, 19(10), 1097–1102. <https://doi.org/10.2337/diacare.19.10.1097>
- Glise, K., Ahlborg, G., Jr., & Jonsdottir, I. H. (2014). Prevalence and course of somatic symptoms in patients with stress-related exhaustion: Does sex or age matter. *BMC Psychiatry*, 14(1), 118. <https://doi.org/10.1186/1471-244X-14-118>
- Grossi, G., Perski, A., Evengård, B., Blomkvist, V., & Orth-Gomér, K. (2003). Physiological correlates of burnout among women. *Journal of Psychosomatic Research*, 55(4), 309–316. [https://doi.org/10.1016/s0022-3999\(02\)00633-5](https://doi.org/10.1016/s0022-3999(02)00633-5)
- Honkonen, T., Ahola, K., Pertovaara, M., Isometsä, E., Kalimo, R., Nykyri, E., Aromaa, A., & Lönnqvist, J. (2006). The association between burnout

- and physical illness in the general population – Results from the Finnish Health 2000 Study. *Journal of Psychosomatic Research*, 61(1), 59–66. <https://doi.org/10.1016/j.jpsychores.2005.10.002>
- Kesim, M., et al. (2011). The effects of sertraline on blood lipids, glucose, insulin and HBA1C levels: A prospective clinical trial on depressive patients. *Journal of Research in Medical Sciences*, 16(12), 1525–1531.
- Kivimäki, M., Hamer, M., Batty, G. D., Geddes, J. R., Tabak, A. G., Pentti, J., Virtanen, M., & Vahtera, J. (2010). Antidepressant medication use, weight gain, and risk of type 2 diabetes: a population-based study. *Diabetes Care*, 33(12), 2611–2616. <https://doi.org/10.2337/dc10-1187>
- Leonard, B. E., & Wegener, G. (2020). Inflammation, insulin resistance and neuroprogression in depression. *Acta Neuropsychiatrica*, 32(1), 1–9. <https://doi.org/10.1017/neu.2019.17>
- Lerman, Y., Melamed, S., Shragin, Y., Kushnir, T., Rotgoltz, Y., Shirom, A., & Aronson, M. (1999). Association between burnout at work and leukocyte adhesiveness/aggregation. *Psychosomatic Medicine*, 61(6), 828–833. <https://doi.org/10.1097/00006842-199911000-00017>
- Lundgren-Nilsson, A., Jonsdottir, I. H., Pallant, J., & Ahlberg, G.Jr. (2012). Internal construct validity of the Shirom–Melamed Burnout Questionnaire (SMBQ). *BMC Public Health*, 12(1), 1. <https://doi.org/10.1186/1471-2458-12-1>
- Macchi, C., Favero, C., Ceresa, A., Vigna, L., Conti, D. M., Pesatori, A. C., Racagni, G., Corsini, A., Ferri, N., Sirtori, C. R., Buoli, M., Bollati, V., & Ruscica, M. (2020). Depression and cardiovascular risk-association among Beck Depression Inventory, PCSK9 levels and insulin resistance. *Cardiovascular Diabetology*, 19(1), 187. <https://doi.org/10.1186/s12933-020-01158-6>
- Matthews, D. R., Hosker, J. P., Rudenski, A. S., Naylor, B. A., Treacher, D. F., & Turner, R. C. (1985). Homeostasis model assessment: Insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia*, 28(7), 412–419. <https://doi.org/10.1007/BF00280883>
- McIntyre, R. S., Soczynska, J. K., Konarski, J. Z., & Kennedy, S. H. (2006). The effect of antidepressants on glucose homeostasis and insulin sensitivity: Synthesis and mechanisms. *Expert Opinion on Drug Safety*, 5(1), 157–168. <https://doi.org/10.1517/14740338.5.1.157>
- Melamed, S., Kushnir, T., & Shirom, A. (1992). Burnout and risk factors for cardiovascular diseases. *Behavioral Medicine (Washington, DC)*, 18(2), 53–60. <https://doi.org/10.1080/08964289.1992.9935172>
- Melamed, S., Shirom, A., Toker, S., & Shapira, I. (2006). Burnout and risk of type 2 diabetes: A prospective study of apparently healthy employed persons. *Psychosomatic Medicine*, 68(6), 863–869. <https://doi.org/10.1097/01.psy.0000242860.24009.f0>
- Melamed, S., Shirom, A., Toker, S., Berliner, S., & Shapira, I. (2006). Burnout and risk of cardiovascular disease: Evidence, possible causal paths, and promising research directions. *Psychological Bulletin*, 132(3), 327–353. <https://doi.org/10.1037/0033-2909.132.3.327>
- Persson, P. G., Carlsson, S., Svanström, L., Ostenson, C. G., Efendic, S., & Grill, V. (2000). Cigarette smoking, oral moist snuff use and glucose intolerance. *Journal of Internal Medicine*, 248(2), 103–110. <https://doi.org/10.1046/j.1365-2796.2000.00708.x>
- Rosmond, R. (2003). Stress induced disturbances of the HPA axis: A pathway to Type 2 diabetes? *Medical Science Monitor*, 9(2), RA35–9.
- Rosmond, R., & Björntorp, P. (2000). The hypothalamic–pituitary–adrenal axis activity as a predictor of cardiovascular disease, type 2 diabetes and stroke. *Journal of Internal Medicine*, 247(2), 188–197. <https://doi.org/10.1046/j.1365-2796.2000.00603.x>
- Saltin, B., & Grimby, G. (1968). Physiological analysis of middle-aged and old former athletes. Comparison with still active athletes of the same ages. *Circulation*, 38(6), 1104–1115. <https://doi.org/10.1161/01.cir.38.6.1104>
- Sheiner, E. K., Sheiner, E., Carel, R., Potashnik, G., & Shoham-Vardi, I. (2002). Potential association between male infertility and occupational psychological stress. *Journal of Occupational & Environmental Medicine*, 44(12), 1093–1099. <https://doi.org/10.1097/00043764-200212000-00001>
- Sjörs, A., Jansson, P.-A., Eriksson, J. W., & Jonsdottir, I. H. (2013). Increased insulin secretion and decreased glucose concentrations, but not allostatic load, are associated with stress-related exhaustion in a clinical patient population. *Stress (Amsterdam, Netherlands)*, 16(1), 24–33. <https://doi.org/10.3109/10253890.2012.688082>
- Strikwerda, M., Beulens, J. W., Rimmelzwaal, S., Schoonmade, L. J., van Straten, A., Schram, M. T., Elders, P. J., & Rutters, F. (2021). The association of burnout and vital exhaustion with type 2 diabetes: A systematic review and meta-analysis. *Psychosomatic Medicine*, 83(9), 1013–1030. <https://doi.org/10.1097/PSY.0000000000000995>
- Tabák, A. G., Herder, C., Rathmann, W., Brunner, E. J., & Kivimäki, M. (2012). Prediabetes: A high-risk state for diabetes development. *Lancet*, 379(9833), 2279–2290. [https://doi.org/10.1016/S0140-6736\(12\)60283-9](https://doi.org/10.1016/S0140-6736(12)60283-9)
- Toker, S., Shirom, A., Shapira, I., Berliner, S., & Melamed, S. (2005). The association between burnout, depression, anxiety, and inflammation biomarkers: C-reactive protein and fibrinogen in men and women. *Journal of Occupational Health Psychology*, 10(4), 344–362. <https://doi.org/10.1037/1076-8998.10.4.344>
- Weber-Hamann, B., Gilles, M., Lederbogen, F., Heuser, I., & Deuschle, M. (2006). Improved insulin sensitivity in 80 nondiabetic patients with MDD after clinical remission in a double-blind, randomized trial of amitriptyline and paroxetine. *Journal of Clinical Psychiatry*, 67(12), 1856–1861. <https://doi.org/10.4088/jcp.v67n1204>
- Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica*, 67(6), 361–370. <https://doi.org/10.1111/j.1600-0447.1983.tb09716.x>