

**Stressful life events and the metabolic syndrome:
The PPP-Botnia Study**

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Running title: Stress and the metabolic syndrome

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Submitted 4 June 2009 and accepted 20 October 2009.

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Objective. Stress may play a role in the pathogenesis of the metabolic syndrome (MetS). However, the scant evidence available is not population-based, restricting external validity of the findings. Our aim was to test associations between stressful life events, their accumulation and the MetS in a large population-based cohort. We also tested associations between stress and the individuals components related to the MetS.

Research Design and Methods. A population-based, random sample of 3,407 women and men aged 18–78 years residing in the Western Finland. Metabolic syndrome was defined according to the ATP III and IDF criteria. Severity of 15 stressful life events pertaining to finance, work, social relationships, health and housing was self-rated.

Results. In comparison to subjects not reporting any extremely stressful life events, those reporting work- or finance-related events had an increased odds for having the MetS. The risk was further increased according to accumulation of stressful finance-related events and to having at least three stressful life events in any of the life domains assessed. Accumulation of stressful life events was associated with insulin resistance, obesity and triglycerides. The associations were not confounded by sex, age, lifestyle or family history of diabetes.

Conclusions. Life events perceived as stressful, particularly those related to finance and work, may signal for poor metabolic health.

Metabolic syndrome (MetS) refers to a cluster of aberrations of metabolic origin that increases the risk for morbidity and mortality from type 2 diabetes (1, 2), cardiovascular disease (CVD) (3), and all-cause mortality (1). Features of the MetS include a combination of impaired glucose and lipid metabolism, obesity and hypertension (4-6). Along the world-wide increase in prevalence of the MetS (7), there exists a strong need to identify underlying, causative factors that may render an individual susceptible to the MetS.

The MetS is thought to be multifactorial in origin arising from a combination of genetic and environmental factors (4). Among the plausible environmental factors is psychosocial stress (8). However, research on the importance of stress in the etiology of the MetS is scanty. Vogelzangs et al. (9) found in their cross-sectional cohort study of 2,917 elderly men and women that per each experienced negative life event the odds for having the MetS increased by 13 percent. In a small sample of elderly women and men (10) caregiver stress predicted MetS at follow-up over 15 later. In the Whitehall II study of over 10,000 middle-aged civil servants, chronic work stress predicted higher odds for having the MetS at a follow-up 14 years later (11). In the Pittsburgh Healthy Women Study middle-aged women who experienced life events as extremely stressful had an increased risk for developing the MetS over an average 15 years of follow-up (12). In the same study also marital dissatisfaction, divorce, and widowhood predicted an increased risk for developing the MetS over an average follow-up of 11.5 years (13).

While important, none of the studies so far have been population-based restricting the external validity of the findings: the participants have been recruited from health care beneficiaries (9), from Alzheimer's caregivers (10), from employees of civil

service departments (11) and from initially healthy premenopausal women holding a driver's licence (12, 13). Accordingly, the first major aim of this study was to test associations between severity of stressful life events arising from various life domains and the MetS defined according to the ATP III and IDF clinical criteria in a large population-based sample of women and men residing in Western Finland. The second major aim of our study was to test the significance of stressful life events for the individual components of the MetS.

RESEARCH DESIGN AND METHODS

Participants. The PPP-Botnia Study (Prevalence, Prediction and Prevention of diabetes) is a population-based study in the Botnia region of Western Finland. The study is designed to obtain accurate estimates of prevalence and risk factors for diabetes, impaired glucose tolerance and the MetS in the population aged 18–78 years and to use this information for prediction and prevention of the disease. The current study was initiated in 2004 in 5 centres (Närpes, Malax-Korsnäs, Korsholm, Vasa and Jakobstad). Using the population registry we selected a random sample of subjects aged 18 to 78 years (96,000 subjects) representing on average 9% of the population. The aim is to include altogether 5,000 individuals. This paper reports data from the first 3,621 persons (1,712 men and 1,899 women) of the 6,079 invited (60%). Of them, 17 had at least one of the components of the MetS missing, and 192 did not fill in the stressful life events questionnaire. Altogether, 3,407 (1,618 men and 1,789 women) participants had complete data available on the components of the MetS and life events. They were younger and more educated, reported higher alcohol intake, had less often family history for diabetes and met the ATP III/IDF criteria for MetS less often compared to the entire group ($P < .001$; no

differences were found in sex distribution or frequency of smoking and regular exercise, *p*-values > 0.31). The participants gave their written informed consent. The study protocol has been approved by the ethics committee of Helsinki University Hospital.

Metabolic syndrome. The subjects participated in an oral glucose tolerance test (OGTT) by ingesting 75 g of glucose after a 12-h overnight fast. Subjects with known diabetes and on anti-diabetic medication or with fasting plasma glucose > 10 mmol/l did not take part in the OGTT (*n* = 19). During the OGTT samples for plasma glucose and serum insulin were drawn at 0, 30 and 120 min. Diagnosis of diabetes was based on the results from the OGTT or a history of previously known diabetes. The diagnosis of diabetes was based on the WHO criteria (5). Thus, subjects with a fasting plasma glucose ≥ 7.0 mmol/l and/or 2-h plasma glucose ≥ 11.0 during an OGTT were considered to have diabetes. Subjects with fasting plasma glucose between 6.1 and 6.9 mmol/l were considered to have impaired fasting glucose (IFG) and subjects with fasting plasma glucose < 7.0 mmol/l and 2-h plasma glucose between 7.8 and 11.0 mmol/l to have impaired glucose tolerance (IGT) (5).

Waist circumference was measured with a soft tape on standing subjects midway between the lowest rib and the iliac crest. Fasting blood samples were drawn for the measurement of HDL cholesterol and triglycerides. Two blood pressure recordings were obtained from the right arm of a sitting subject after 10 min of rest, and the mean value was calculated.

We used the ATP III (4) and the IDF criteria (6) to define the MetS. According to the ATP III criteria at least three of the following five criteria have to be met: waist circumference ≥ 102 cm in men and ≥ 88 cm in women, serum triglycerides ≥ 1.7 mmol/l and HDL - cholesterol < 1.0 mmol/l in men and < 1.3 mmol/l in women, IFG/IGT or diabetes, and

blood pressure $\geq 130/85$ mmHg and/or use of anti-hypertensive medication. The IDF clinical criteria include waist circumference ≥ 94 cm in men and ≥ 80 cm in women and an additional two of the following criteria: serum triglycerides ≥ 1.7 mmol/l, HDL cholesterol < 1.03 mmol/l in men and < 1.29 mmol/l in women, blood pressure ($\geq 130/85$ mmHg and/or use of anti-hypertensive medication) or fasting plasma glucose ≥ 5.6 mmol/l.

In addition to the components defined by the ATP III and the IDF, we extended our analyses to using the HOMA_{IR} [(fasting plasma glucose x fasting insulin) / 22.5] (14) as an additional index in insulin resistance and BMI (kg/m² measured with subjects in light indoor clothing and without shoes) as an additional index of general obesity as outcomes.

Assays. Plasma glucose during the OGTT was measured with a glucose dehydrogenase method

(Hemocue, Angelholm, Sweden) and serum insulin by a fluoroimmunoassay (Delphia, Perkin-Elmer Finland, Turku, Finland). Serum HDL cholesterol and triglyceride concentrations were analysed with an enzymatic method on a Konelab 60i analyser (Thermo Electron Oy, Vantaa, Finland).

Stressful life events. The subjects completed a questionnaire consisting of 15 stressful life events (Table 2). All questions concerned life events known to be major stressors (12, 15-17). The subjects were asked to evaluate the occurrence and stressfulness of these events (0 = not occurred, 1 = not at all stressful, 2 = mildly stressful, 3 = moderately stressful, 4 = extremely stressful) during the past 12 months. For the analyses, the measurement scale was dichotomized by contrasting moderately and extremely stressful events (hereafter called as extremely stressful life events) with events that were not at all or mildly stressful or had not occurred at all (hereafter called as no stressful life events) (12).

Mediating and confounding factors. The subjects self-reported their weekly alcohol consumption (g/week), current smoking (yes vs. no or former smoker), regular exercise (yes vs. no), level of education (less than high school, high school or college graduate, degree beyond college) and family history of known diabetes (yes vs. no) in at least one first degree relative (father, mother or sibling).

Statistical analyses. Logistic regression analyses, odds ratios (OR) and 95% confidence intervals (95% CI) were computed to examine associations between stressful life events and the MetS. Multiple linear regression analyses, unstandardized regression coefficients and 95% CI were computed to examine associations between stressful life events and HOMA_{IR}, waist circumference, BMI, triglycerides, HDL cholesterol, SBP and DBP, and logistic regression analyses to examine associations with IFG and IGT. The associations were adjusted for the mediating and confounding factors. Since the unadjusted and fully adjusted models resulted in essentially similar results, we present the fully adjusted associations only. Finally, because associations between psychosocial factors and the MetS may be moderated by sex (9, 10), we tested if any of the associations varied for men and women by including an interaction term, 'sex x extremely stressful life event' in the models. Tests of moderation by sex were also supported by our own data demonstrating a preponderance for women to report more life events as extremely stressful in all the measured life domains (Online Appendix Tables A1 and A2 which is available at <http://care.diabetesjournals.org>). In no instance, was there a significant sex - interaction -term (p-values > .07) (data not shown). For this reason we report the results in both sexes combined.

RESULTS

Table 1 shows that the agreement rate between the ATP III and the IDF criteria was high. Consequently, the ATP III and the IDF criteria resulted in similar differences between the groups meeting and not meeting the MetS in biological, socio-demographic and lifestyle characteristics and in family history of diabetes. Therefore, characteristics of the sample are presented according to the ATP III criteria only (Table 1).

Stressful life events and the MetS. Table 2 shows that the odds for having the MetS according to the ATP III, the IDF or both criteria was significantly higher among participants who had experienced extremely stressful life events in finance-, (ongoing financial strain, severe financial strain, threat of unemployment or personal bankruptcy), work-, (troubles with co-workers, beginning a new job) and health- related domains (concern over own or child's ability to cope with stress).

Further, the odds for having the MetS according to the ATP III and the IDF criteria was significantly higher among participants who had experienced at least one stressful life event in the finance -related domain, and at least three events in any of the life domains (Table 3).

Stressful life events and components of the MetS. Analyses of the components of the MetS indicated that participants who had experienced stressful life events in the finance-, work-, and health-related domains or had experienced at least three events in any of the life domains displayed higher levels of HOMA_{IR}, waist circumference, BMI, triglycerides, and had a higher odds for having IGT (Table 4). Stress did not associate significantly with IFG, HDL cholesterol or BP (data not shown).

CONCLUSIONS

The key finding in the present study is that individuals who reported extremely stressful life events within finance- and work-related

life domains had significantly higher odds for having the MetS. The risk was further increased according to accumulation of stressful finance-related events and according to having at least three events in any of the life domains we measured, namely finance, work, social relationships, health and housing. Accumulation of stressful finance-, and work-related life events and having at least three stressful events in any of the life domains associated significantly also with insulin resistance, obesity and triglycerides. The associations were not confounded by sex, age, lifestyle or family history of diabetes.

Our findings are in agreement with previous studies (9-13) by showing that major stress-related events associate with an increased risk for having the MetS. However, our findings further suggest that out of the life events we measured, those relating more specifically to finance and work seemed the most harmful. While chronic work stress has been associated with an increased risk for having the MetS in the Whitehall II study (11), the other existing studies have not specifically focused on work-related stress and none of the studies on finance-related stress, precluding direct comparisons between the studies.

Our findings with the different components of the MetS agree well with the work and hypothesis put forward by Björntorp (8). According to Björntorp, hypothalamic-pituitary-adrenocortical (HPA) axis abnormality may contribute to both insulin resistance and abdominal obesity with lipids and blood pressure being the secondary complications (8). In addition to alcohol and smoking, among the major triggers of this chain of events is psychosocial stress of a 'defeat', 'helpless' type (8). While the cross-sectional nature of our study precludes any inferences about causality, it is indeed interesting that we found that major stressful life events associated most closely with indices of insulin resistance, obesity and triglycerides. To our knowledge, one previous

study has shown that accumulation of non-work –related stressful life events were associated with increased risk of obesity in men, higher waist-hip-ratio in women and men, but not with fasting insulin concentrations (17), findings that are at least partly in line with the current ones.

Apart from the HPA axis abnormality, other mechanisms that may underlie these associations include autonomic nervous system (ANS) and inflammatory activity (4, 8, 18). Alterations in these physiological systems are linked with the MetS, insulin resistance and obesity (19). By inducing changes in lifestyle stress may associate with metabolic changes through smoking, alcohol use and physical inactivity. Our associations were not, however, affected by controls of lifestyle. Neither were the associations affected by educational attainment or by a family history of diabetes. Finally, stress may induce changes in other psychosocial risk factors, such as sleep pattern (20) and depression (21). As poor sleep and depression are associated with the MetS (12, 22), insulin resistance (23, 24), and diabetes (24, 25), these may provide additional pathways through which stress is related to the MetS. Furthermore, we cannot rule out genetic pathways. While specific genetic markers cannot be nominated, these may relate to glucocorticoids, catecholamines and inflammatory markers, or to yet an unknown novel genetic marker.

The strengths of this study lie in the population-based study design, detailed clinical examination and measurement of stressful life events and their severity across various life domains. All of these strengths contribute significantly to the existing literature. None of the prior studies testing associations between stress and the MetS have been population-based restricting the external validity of the findings. None of the prior studies has measured insulin and glucose after an oral glucose challenge

precluding more precise definitions of the MetS and focus on glucose tolerance. Except for one (12), none of the studies has measured the perceived severity of the stressful life events. Different events may pose different experiences in different individuals, thus separating out the perceived severity of different events (not equating events per se, such as death of a spouse, death of a pet) is important. Also, our study offered sufficient power to test sex-specificity of the associations. While the association between some psychosocial factors and MetS has been reported to be different in men than in women (9, 10), our data did not reveal any such differences.

Apart from a cross-sectional study design, another limitation of the study is that the sample is composed of white Caucasians only. Thus, the findings may not generalize to groups with other ethnic backgrounds. Further, 5.9% of our study population were excluded because of missing information, the major reason being missing data in life events questionnaire (5.3%). Those with full information, compared to those without, were younger, more educated, consumed more alcohol, had less frequently a family history of diabetes and met the criteria for MetS less frequently. However, a bias towards inclusion of younger, more educated and healthier participants might diminish rather than increase our ability to detect significant associations. We measured occurrence and severity of stressful life events the past 12 months. Yet, we cannot determine the precise timing and duration of the life events, and hence cannot address the temporal relationships between stress and health in any further detail. Stressful life events and psychiatric disorders, such as major depression, are associated (21). As we did not have data available on psychiatric disorders, we cannot rule out that these may explain the associations. Finally, while all the

associations were adjusted for level of education as a proxy of social position, a possibility remains that for a specific subgroup adjusting for level of education may not have been sufficient in capturing the overlap that may exist in social position and some of the stressful events.

To aggregate, our study shows that extremely stressful life events, particularly those related to finance and work, are associated with increasing odds for having the MetS and with having higher degrees of insulin resistance, obesity and triglycerides. Our study was conducted before the global economic crisis. Thus, if finance- and work-related troubles play a role in the pathogenesis increasing the risk for the MetS, we can only speculate that over the next decade we may see an increase in the prevalence of the MetS and associated disease.

ACKNOWLEDGEMENTS

The PPP-Botnia study has been financially supported by grants from the Sigrid Juselius Foundation, Folkhälsan Research Foundation, Nordic Center of Excellence in Disease Genetics, Signe and Ane Gyllenberg Foundation, Swedish Cultural Foundation in Finland, Finnish Diabetes Research Foundation, Foundation for Life and Health in Finland, Finnish Medical Society, Ministry of Education, Paavo Nurmi Foundation, Perklén Foundation, Ollqvist Foundation and Närpes Health Care Foundation. The study has also been supported by the Municipal Health Care Center and Hospital in Jakobstad, Health Care Centers in Vasa, Närpes and Korsholm. The skilful assistance of the Botnia Study Group is gratefully acknowledged.

The authors (KR; A-JP, TT, JGE, BI) declare no conflict of interest. Leif Groop has been a consultant for and served on advisory boards for Sanofi-Aventis, GSK, Novartis, Merck, Tethys Bioscience and Xoma and received lecture fees from Lilly and Novartis.

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Table 1. Characteristics of the sample according to the National Cholesterol Education Program Adult Treatment Panel III (ATP III) clinical criteria of the MetS.

Characteristic:	ATP III		P for a difference between groups
	No, n = 2693	Yes, n = 714	
IDF clinical criteria, yes, n (%)	391 (14.5)	675 (94.5)	0.001
Sex, men, n (%)	1260 (46.8)	358 (50.1)	0.111
Age (years)	46.5 ± 15.9	56.5 ± 12.8	0.001
Fasting glucose (mmol/l)	5.2 ± 0.8	5.8 ± 1.3	0.001
Glucose 30 min. (mmol/l)	8.1 ± 1.6	9.4 ± 2.0	0.001
Glucose 120 min. (mmol/l)	5.0 ± 1.6	6.8 ± 3.0	0.001
HOMA_{IR} index *	1.35 ± 1.39	3.19 ± 4.76	0.001
Waist circumference (cm)	85.3 ± 11.1	102.0 ± 11.2	0.001
Body Mass Index (kg/m²)	25.2 ± 3.5	30.7 ± 4.5	0.001
Triglycerides (mmol/l)	1.1 ± 0.5	2.1 ± 1.1	0.001
HDL cholesterol (mmol/l)	1.44 ± 0.36	1.10 ± 0.27	0.001
SBP (mmHg)	131 ± 19	146 ± 19	0.001
DBP (mmHg)	79 ± 10	86 ± 9	0.001
Current smoker, yes, n (%)	393 (14.7)	123 (17.7)	0.056
Regular exercise, yes, n (%)	1492 (55.9)	332 (47.1)	0.001
Alcohol consumption, n (%)			
None	664 (25.6)	232 (34.2)	0.001
12-48 g/wk	1233 (47.5)	282 (41.6)	
60 ≥ g/wk	701 (27.0)	164 (24.2)	
Level of Education, n (%)			
Less than high school	1821 (67.7)	605 (84.7)	0.001
High school or college degree	439 (16.3)	50 (7.0)	
Degree beyond college	430 (16.0)	59 (8.3)	
Family history for diabetes, yes, n (%)	733 (29.1)	292 (45.0)	0.001

* Fasting plasma insulin (μU/ml) x fasting plasma glucose level (mmol/l)/22.5

Table 2. Fully adjusted (sex, age, alcohol consumption, current smoking status, regular exercise, level of education and family history of diabetes) associations between stressful life events during the past 12 months and the MetS according to the National Cholesterol Education Program Adult Treatment Panel III (ATP III) and the International Diabetes Foundation (IDF) criteria.

No (n = 2,296) versus extremely stressful life events:	ATP III		IDF	
	Odds ratio (95% CI)	<i>P</i>	Odds ratio (95% CI)	<i>P</i>
Finance				
1. Ongoing financial strain (n=213)	1.60 (1.07–2.39)	0.023	1.24 (0.85–1.81)	0.267
2. Severe financial strain, laid off business (n=100)	2.80 (1.69–4.63)	0.001	2.10 (1.29–3.42)	0.003
3. Threat of unemployment or personal bankruptcy (n = 89)	2.90 (1.70–4.94)	0.001	1.95 (1.16–3.27)	0.012
Work				
4. Continuous work overload (n=318)	1.17 (0.83–1.65)	0.381	1.15 (0.85–1.56)	0.361
5. Troubles with co-workers (n=167)	1.79 (1.17–2.75)	0.007	1.75 (1.18–2.59)	0.005
6. Began a new job (n= 42)	2.29 (1.05–4.98)	0.037	1.93 (0.92–4.02)	0.081
Social relationships				
7. Ongoing difficulties in close relationships (n=160)	0.95 (0.56–1.62)	0.856	0.86 (0.54–1.37)	0.521
8. Divorced or separated from husband/wife/partner (n=153)	1.44 (0.90–2.31)	0.127	1.31 (0.85–2.01)	0.220
9. Death of spouse/partner/close friend (n=224)	1.17 (0.79–1.72)	0.431	1.07 (0.75–1.53)	0.692
Health				
10. Serious injury or illness (n =194)	1.29 (0.87–1.91)	0.210	1.15 (0.80–1.66)	0.454
11. Concern over health of a family member or a close friend (n=376)	1.20 (0.88–1.62)	0.246	1.07 (0.81–1.42)	0.609
12. Concern over own or child's ability to cope with stress (n=210)	1.59 (1.11–2.28)	0.012	1.26 (0.89–1.79)	0.186
Housing				
13. Loss of home (n=26)	1.67 (0.61–4.55)	0.314	1.84 (0.68–4.97)	0.232
14. Change of residence (n=58)	1.22 (0.53–2.82)	0.643	1.13 (0.53–2.42)	0.758
15. Difficulties in housing (n=22)	2.51 (0.89–7.05)	0.081	1.80 (0.65–5.03)	0.261

Note. No stressful life events refer to a category combining individuals who report no stressful life events or life events that are not at all or mildly stressful; Extremely stressful life events refer to a category combining individuals who report moderately or extremely stressful life events; Number of individuals in parenthesis refer to the number reporting extremely stressful life events.

Table 3. Fully adjusted (sex, age, alcohol consumption, current smoking status, regular exercise, level of education and family history of diabetes) associations between accumulation of stressful life events during the past 12 months and the metabolic syndrome according to the National Cholesterol Education Program Adult Treatment Panel III (ATP III) and the International Diabetes Foundation (IDF) criteria.

No (n = 2,296) versus accumulation of extremely stressful life events:	ATP III		IDF	
	Odds ratio (95% CI)	P	Odds ratio (95% CI)	P
Finance				
at least 1 event (n = 273)	1.78 (1.25–2.53)	0.001	1.42 (1.03–1.98)	0.036
at least 2 events (n = 98)	2.91 (1.75–4.89)	0.001	1.85 (1.12–3.05)	0.016
at least 3 events (n = 31)	4.08 (1.66–10.06)	0.002	2.82 (1.15–6.92)	0.023
Work				
at least 1 event (n = 421)	1.34 (0.99–1.81)	0.061	1.30 (0.99–1.70)	0.058
at least 2 events (n = 97) *	1.70 (0.99–2.92)	0.055	1.63 (0.99–2.66)	0.053
Social relationships				
at least 1 event (n = 425)	1.13 (0.83–1.53)	0.447	1.06 (0.81–1.40)	0.666
at least 2 events (n = 98) †	1.56 (0.88–2.75)	0.125	1.25 (0.73–2.14)	0.419
Health				
at least 1 event (n = 592)	1.23 (0.96–1.59)	0.101	1.12 (0.89–1.41)	0.347
at least 2 events (n = 155)	1.65 (1.10–2.50)	0.016	1.27 (0.85–1.88)	0.240
at least 3 events (n = 33)	1.45 (0.63–3.34)	0.378	1.06 (0.47–2.40)	0.888
Housing				
at least 1 event (n = 86) ‡	1.56 (0.84–2.91)	0.163	1.36 (0.76–2.45)	0.304
Across all life domains				
at least 1 event (n = 1111)	1.21 (0.98–1.49)	0.075	1.09 (0.90–1.31)	0.395
at least 2 events (n = 583)	1.42 (1.10–1.84)	0.008	1.16 (0.91–1.47)	0.225
at least 3 events (n = 300)	1.64 (1.18–2.28)	0.003	1.47 (1.08–1.99)	0.013
at least 4 events (n = 174)	1.91 (1.28–2.86)	0.002	1.81 (1.24–2.64)	0.002
at least 5 events (n = 88)	2.23 (1.31–3.81)	0.003	1.78 (1.06–2.98)	0.028
at least 6 events (n = 45) §	2.95 (1.43–6.11)	0.004	2.70 (1.32–5.52)	0.007

Note. No stressful life events refer to a category combining individuals who report no stressful life events or life events that are not at all or mildly stressful; Extremely stressful life events refer to a category combining individuals who report moderately or extremely stressful life events; Number of individuals in parenthesis refer to number reporting extremely stressful life events; * Number of participants reporting at least 3 events was 9, therefore this category is not analysed separately; † Number of participants reporting at least 3 events was 14, therefore this category is not analysed separately; ‡ Number of participants reporting at least 2 events was 20, therefore this category is not analysed separately; § Number of participants reporting at least 7 events was 25, therefore this category is not analysed separately.

Table 4. Fully adjusted (sex, age, alcohol consumption, current smoking status, regular exercise, level of education and family history of diabetes) associations between accumulation of stressful life events during the past 12 months and insulin resistance, obesity and triglycerides.

No (n = 2,296) Versus accumulation of extremely stressful life events:	Impaired glucose tolerance (no vs. yes)		Log of HOMA _{IR} *		Waist Circumference		Body Mass Index		Log of Triglycerides	
	Odds ratio (95% CI)	P	% change (95% CI)	P	Change in cm (95% CI)	P	Change in kg/m ² (95% CI)	P	% change (95% CI)	P
Finance										
at least 1 event (n= 273)	1.71 (0.93–3.16)	0.085	10.03 (0.40–19.65)	0.041	2.30 (0.86–3.74)	0.002	0.95 (0.40–1.51)	0.001	7.65 (1.18–14.11)	0.020
at least 2 events (n= 98)	3.27 (1.45–7.33)	0.004	24.20 (8.67–39.72)	0.002	3.82 (1.49–6.14)	0.001	1.23 (0.34–2.11)	0.007	12.07 (1.80–22.34)	0.021
at least 3 events (n = 31)	5.65 (1.51–21.19)	0.010	35.61 (5.99–65.22)	0.018	8.64 (4.32–12.96)	0.001	3.91 (2.26–5.55)	0.001	25.75 (6.62–44.88)	0.008
Work										
at least 1 event (n= 421)	1.54 (0.91–2.60)	0.106	3.89 (-3.97–11.76)	0.332	1.60 (0.44–2.76)	0.007	0.63 (0.20–1.07)	0.005	6.33 (1.14–11.53)	0.017
at least 2 events (n= 97) †	2.78 (1.20–6.48)	0.018	12.15 (-3.01–27.30)	0.116	3.15 (0.92–5.37)	0.006	1.26 (0.41–2.10)	0.004	13.38 (3.43–23.34)	0.008
Social relationships										
at least 1 event (n= 425)	1.41 (0.87–2.27)	0.162	2.21 (-5.71–10.13)	0.584	0.73 (-0.46–1.92)	0.228	0.39 (-0.06–0.84)	0.091	1.52 (-3.75–6.80)	0.571
at least 2 events (n= 98) ‡	2.47 (1.09–5.60)	0.031	17.04 (1.48–32.60)	0.032	0.24 (-2.07–2.55)	0.837	0.11 (-0.77–0.99)	0.809	10.10 (-0.17–20.37)	0.054
Health										
at least 1 event (n= 592)	1.56 (1.07–2.28)	0.022	4.91 (-1.92–11.73)	0.159	0.80 (-0.24–1.84)	0.133	0.47 (0.07–0.86)	0.021	-1.88 (-6.51–2.74)	0.425
at least 2 events (n= 155)	1.81 (0.99–3.30)	0.054	15.37 (2.87–27.88)	0.016	1.87 (0.01–3.73)	0.048	1.12 (0.42–1.83)	0.002	4.36 (-3.85–12.57)	0.297
at least 3 events (n= 33)	1.07 (0.30–3.83)	0.923	32.13 (6.39–57.87)	0.014	1.84 (-1.96–5.65)	0.342	1.20 (-0.24–2.63)	0.102	10.12 (-6.84–27.08)	0.242
Housing										
at least 1 event (n= 86) §	4.06 (1.88–8.74)	0.001	27.25 (10.39–44.11)	0.002	3.48 (0.97–5.99)	0.007	1.66 (0.70–2.61)	0.001	10.57 (-0.52–21.66)	0.062
Across all life domains										
at least 1 event (n= 1111)	1.43 (1.03–1.98)	0.033	3.17 (-2.28–8.62)	0.254	1.12 (0.29–1.95)	0.008	0.59 (0.27–0.91)	0.001	0.46 (-3.23–4.15)	0.805
at least 2 events (n= 583)	1.72 (1.15–2.57)	0.008	6.06 (-0.88–12.99)	0.087	1.22 (0.16–2.27)	0.024	0.59 (0.19–1.00)	0.004	3.25 (-1.44–7.93)	0.175
at least 3 events (n= 300)	1.94 (1.17–3.22)	0.010	13.72 (4.55–22.88)	0.003	2.50 (1.11–3.88)	0.001	1.18 (0.65–1.71)	0.001	6.88 (0.80–12.97)	0.027
at least 4 events (n= 174)	2.70 (1.51–4.85)	0.001	21.79 (10.09–33.48)	0.001	2.72 (0.96–4.48)	0.002	1.18 (0.51–1.85)	0.001	13.14 (5.35–20.92)	0.001
at least 5 events (n= 88)	2.66 (1.18–6.00)	0.018	25.85 (9.82–41.87)	0.002	3.07 (0.69–5.45)	0.011	1.09 (0.19–1.98)	0.018	16.79 (6.20–27.37)	0.002
at least 6 events (n= 45)	2.77 (0.88–8.68)	0.081	36.09 (13.29–58.88)	0.002	4.19 (0.83–7.54)	0.014	1.22 (-0.04–2.48)	0.058	22.04 (7.14–36.94)	0.004

Note. No stressful life events refer to a category combining individuals who report no stressful life events or life events that are not at all or mildly stressful; Extremely stressful life events refer to a category combining individuals who report moderately or extremely stressful life events; Number of individuals in parenthesis refers to the number in the extremely stressful life events category; Associations between stressful life events and impaired glucose tolerance (no vs. yes) were tested using logistic regression analyses and therefore odds ratios are presented; All the other associations were tested using linear regression analyses. The scales of HOMA_{IR} and triglycerides were skewed. Therefore, they were log-transformed for the analyses and their units are presented as percents; * Fasting plasma insulin ($\mu\text{U/ml}$) x fasting plasma glucose level (mmol/l)/22.5; † Number of participants reporting at least 3 events was 9, therefore this category is not analysed separately; ‡ Number of participants reporting at least 3 events was 14, therefore this category is not analysed separately; § Number of participants reporting at least 2 events was 20, therefore this category is not analysed separately; || Number of participants reporting at least 7 events was 25, therefore this category is not analysed separately.