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Perceived stress, multimorbidity, and use of primary care health services

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Abstract

Objectives

Mental stress is common in the general population. Mounting evidence suggests that mental stress is associated with multimorbidity, suboptimal care, and increased mortality. Delivering healthcare in a bio-psycho-social context is key for general practitioners (GPs), but it remains unclear how persons with high levels of perceived stress are managed in primary care. Our aim was to describe the association between perceived stress and primary care services by focussing on mental health related activities and markers of elective/acute care while accounting for mental-physical multimorbidity.

Design

Population-based cohort study.

Setting

Primary health care in Denmark.

Participants

118,410 participants from the Danish National Health Survey 2010 followed for one year. Information on perceived stress and lifestyle was obtained from a survey questionnaire. Information on multimorbidity was obtained from health registers.

Outcome measures

General daytime consultations, out-of-hours services, mental health related services, and chronic care services in primary care obtained from health registers.

Results

Perceived stress levels were associated with primary care activity in a dose-response relation when adjusted for underlying conditions, lifestyle, and socioeconomic factors. In the highest stress quintile, 6.8% received GP talk therapy (highest versus lowest quintile, adjusted incidence rate ratios (IRR): 4.96, 95% CI: 4.20–5.86), 3.3% consulted a psychologist (IRR: 6.49, 95% CI: 4.90–8.58), 21.5% redeemed an

antidepressant prescription (IRR: 4.62, 95% CI: 4.03–5.31), 23.8% received annual chronic care consultations (IRR: 1.22, 95% CI: 1.16–1.29), and 26.1% used out-of-hours services (IRR: 1.47, 95% CI: 1.51–1.68). For those with multimorbidity, stress was associated with more out-of-hours services, but not with more chronic care services.

Conclusion

Persons with high stress levels generally had higher use of primary health care, 4–6 times higher use of mental health related services (most often in the form of psychotropic drug prescriptions), but less timely use of chronic care services.

Keywords (MeSH): stress, psychological; practice patterns, physicians'; primary health care; family practice; general practice; comorbidity

Article summary

Strengths and limitations of this study

- Mental stress is common and detrimental for the health, but little is known about the management of persons with high levels of perceived stress in primary care.
- This is the first population-based cohort study to investigate the association between stress perception and general practice utilization taking multimorbidity into account.
- In total, 118,410 persons who participated in the Danish National Health Survey of 2010 and filled out the Perceived Stress Scale questionnaire were followed, and information on daytime services, out-of-hours services, chronic care services, and mental health related services were obtained from national health registries.
- Multimorbidity was assessed using register-based data on diagnoses and medicine prescriptions of 39 mental and physical conditions.
- Limitations of this study include the lack of non-respondents' stress data, lack of private practice psychologist service data, and no access to GP medical records to explore details of provided services and diagnoses.

Introduction

Mental stress is common in the general population[1,2] and an increasingly common reason for contacting the general practitioner (GP).[3] Persons with high levels of perceived stress have higher physical disease burden, impaired prognosis of physical disease, more potentially preventable hospitalisations, and higher mortality than persons with low levels of perceived stress, even after adjusting for mental-physical multimorbidity.[2,4] However, little is known about the services provided by GPs and other health professionals in primary care to persons with high levels of perceived stress. No official treatment guidelines exist, and the care may differ depending on the burden of mental and physical comorbidities.

We aimed to describe the frequency of daytime and out-of-hours contacts according to perceived stress level and multimorbidity status in a large population-based cohort based on health registry data and information on perceived stress and lifestyle measures. Specifically, we focused on mental health related primary care services, psychotropic medication, and selected markers of the balance between elective chronic care and acute out-of-hours services.

Methods

Study population, design and setting

The study population consisted of respondents (age > 25 years) from the nationwide Danish National Health Survey of 2010.[5] Survey questionnaires were collected by 1 May 2010 (index date). We excluded persons who died or emigrated before this date (2,235 persons). A total of 118,410 (response rate: 56%) returned the questionnaire with information on all perceived stress items.

We conducted a population-based cohort study with follow-up until death, emigration, or end-of-study after one year (1 May 2011), whichever came first. Using the personal identification number assigned to all Danish citizens,[6] we linked individual-level data across survey responses and health registers. Almost all Danish citizens are listed with a GP providing them with universal tax-funded access to health care.[7] The GP acts as a gatekeeper to secondary care[8] and may refer to other publicly funded services in primary care. Referrals to private practice psychiatrists are fully covered by the health care system. Referrals to psychologists are partly covered if certain criteria are fulfilled, e.g. a diagnosis of depression or anxiety, or loss of a first-degree relative, but not high perceived stress in itself.

Perceived stress

In the survey questionnaire, perceived stress was measured using Cohen's widely used validated Perceived Stress Scale (PSS).[9-11] The PSS is based on a five level Likert-style questionnaire with items on general stress, coping, and feeling of control. The 10-item Danish version produces a sum score of 0–40; 40 points represent the highest perceived stress level. The stress score was divided into quintiles to assess potential non-linear relations with outcomes.

Multimorbidity

The participant's health status on the index date was assessed using a multimorbidity index of eight psychiatric and 31 physical long-term conditions (eTable 1) identified in nationwide health registers by a previously described algorithm.[2] Multimorbidity was defined as two or more coexisting conditions.[12]

Outcomes

Our main outcomes of interest were categorised into two groups: 1) services related to mental health (GP talk therapy, GP psychometric tests, and sessions with a publicly reimbursed private practicing psychologist or psychiatrist) and redemption of psychotropic medication, 2) services in general practice related to elective chronic care (spirometry test for lung disease, blood sugar sampling for diabetes, electrocardiograms (ECGs) and home blood pressure monitoring for cardiovascular disease, and annual chronic care consultations [a single annual review meeting per chronic disease per patient]), and out-of-hours services (telephone or face-to-face contact with GP). We also assessed the overall rate of daytime face-to-face contacts with GPs.

The Danish National Health Service Register provided data on all publicly reimbursed services performed by Danish GPs, psychologists, and psychiatrists.[13] The Danish National Prescription Registry provided data on redeemed drug prescriptions from all Danish pharmacies.[14] Service codes and "Anatomical Therapeutic Chemical" (ATC) medication codes used to identify the outcomes can be found in the Appendix (eTable 2).

Other covariates

Information on highest achieved education level according to the UNESCO classification system,[15] cohabitation status, and ethnicity was obtained from Statistics Denmark.[16] The Danish Civil Registration System provided information on sex, age, and vital status.[6] Information on working status and lifestyle factors (physical activity, body mass index, and alcohol, smoking, and dietary habits) was obtained from the survey.

Statistical analysis

Cumulative incidence proportions (CIPs) at one year after the index date and incidence rates (IRs) during follow-up were calculated for all investigated primary care activities. We used a negative binomial regression model to calculate incidence rate ratios (IRRs) by PSS score quintiles and assigned the first PSS quintile as the reference. We then adjusted for sex, age as 10-year age bands, presence of each of the 39 conditions in the multimorbidity index, lifestyle factors, and socioeconomic factors on the index date. We included the time at risk to account for death or immigration in both models. Cluster robust variance estimation was used to estimate 95% confidence intervals (95% CIs) to account for inter-individual heterogeneity. We imputed missing data on lifestyle and socioeconomic factors in a chained equations model of all our analysis parameters and produced 20 imputation sets.[17] To assess the effect modification from disease burden, we stratified the analyses on the number of the 31 physical conditions of the multimorbidity index.

The sensitivity analyses included: 1) analysis including only persons without psychiatric illness, 2) analyses of general primary care outcomes by survey response status using register-based information and psychiatric illness as a proxy for stress, and 3) complete-case analysis excluding persons with missing data.

All analyses were performed using Stata 13.1 (StataCorp, College Station, TX).

The study has been performed in accordance with the STROBE guidelines.

Results

The median age was 54 years (interquartile range: 23 years). The median PSS score was 11. Within the one year of follow-up, the study population was at risk for 117,856 person-years. A total of 1,042,353 reimbursed primary care services and 85,962 redeemed psychotropic prescriptions of interest were

recorded. The perceived stress levels were generally higher for women and tended to increase with increasing number of physical conditions and presence of psychiatric morbidity (Table 1). The distribution of survey variables across PSS quintiles has been reported elsewhere.[2]

For all primary care activities, except home blood pressure monitoring, a dose-response relation seemed to exist between the perceived stress level and the probability of receiving a primary care service or psychotropic prescription during follow-up (Tables 2 and 3, 1-year CIPs). The highest IRRs associated with perceived stress were found for mental health related activities, but adjustments attenuated the association (Table 2, IRRs). Among the highest stress quintile, 6.8% received GP talk therapy (highest versus lowest PSS quintile; adjusted IRR: 4.96, 95% CI: 4.20–5.86), 3.3% consulted a psychologist (IRR: 6.49, 95% CI: 4.90–8.58), 3.7% consulted a psychiatrist (IRR: 13.26, 95% CI: 8.33–21.09), 21.5% redeemed an antidepressant prescription (IRR: 4.62, 95% CI: 4.03–5.31), 23.8% received annual chronic care consultations (IRR: 1.22, 95% CI: 1.16–1.29) and 26.1% used out-of-hours services (IRR: 1.47, 95% CI: 1.51–1.68). The proportion of persons who visited their GP at least once during the follow-up year rose with increasing stress levels from 77% to 89% (Table 3).

The IRRs for receiving a mental health related service generally remained stable across PSS quintiles, regardless of underlying disease count (Figure 1, IRRs). However, in absolute terms, the use of talk therapy and psychologist services decreased and psychotropic drug prescriptions increased with increasing numbers of physical conditions (Figure 1, 1-year CIP).

Nearly all persons with physical multimorbidity visited their GP during the investigated year. Multimorbidity in itself was associated with use of elective chronic care services, i.e. annual chronic care consultations, blood sugar measures, ECGs and home blood pressure monitoring (Figure 2). In those with multimorbidity, higher stress levels were not associated with more elective chronic care services than lower stress levels. In absolute numbers, the use of chronic care services tended to decrease with

increasing stress level. Stress was generally associated with use of acute out-of-hours services, regardless of multimorbidity level, but those with multimorbidity tended to have higher use (Figure 2).

Sensitivity analyses

Excluding persons with psychiatric illness from the analyses did not change the overall pattern of primary care activities (eTable 3). The non-response analyses showed that survey non-respondents more often were men and mentally ill (p<0.001) and less often used daytime consultations and services related to chronic care (eTable 4). The adjusted IRRs of general primary care services were similar, regardless of response status when using psychiatric illness as a proxy for high levels of perceived stress (eTable 5). The complete case analysis showed virtually no differences from our main analysis with multiple imputed data (data not shown).

Discussion

Summary

This population-based cohort study showed that the primary care activities increased with increasing perceived stress levels, even after adjusting for co-existing mental and physical conditions, lifestyle, and socioeconomic factors. However, few persons with high levels of perceived stress received mental health services, and more persons received psychotropic medication prescriptions than talk therapy. The rate of preventive services, e.g. annual chronic care consultations and disease monitoring tests, did not increase with increasing stress levels in persons with multimorbidity. Most persons with high stress

levels were in contact with their GP during the investigated year and had higher use of out-of-hours services than those with low stress levels.

Strengths and limitations

This study was based on unique information on stress levels and lifestyle factors in a large random sample of the Danish background population. The Danish Civil Registration System[6] allowed us to link information across health care registers and ensured no loss to follow-up.

Non-respondents tended to be different from survey respondents. Therefore, the absolute number of contacts to primary health care in our study may not be generalisable to the whole population. However, we have no reason to believe that response status affected the adjusted association between perceived stress and use of primary health care as the service use was similar among respondents and non-respondents using a proxy for stress.

Danish health register data are prospectively recorded and validated; these data are considered to be of high quality.[6,13,14] All GPs report their patients' service use, and all pharmacies report redeemed prescriptions.[7] As reporting of primary care services is economically incentivised, high completeness is expected.[13] Reporting may be incomplete if the GP forgets to register a service (e.g. talk therapy). However, the GP's reporting is probably unaffected by patient stress levels; a potential misclassification is thus non-differential. Patients with more severe or complicated chronic disease may be followed in outpatient clinics and have fewer GP chronic care visits. If stress level was a marker of disease severity, this may explain the lack of association between stress and chronic care services among persons with multimorbidity. Psychologist services are probably well recorded in the health registers for reimbursement purposes, whereas visits payed by e.g. insurance companies and municipal or private

organisations are not; the use of psychologists may hence be underestimated in our study. The lack of a Danish register for primary care diagnoses meant that multimorbidity status was based on outpatient and hospital discharge diagnoses combined with recordings of repeated prescriptions. This provided us with information on chronic conditions commonly managed in primary care, but the capture may not be complete.[2]

The combined data sources from survey and registers allowed us to adjust for demographic, lifestyle, and socioeconomic confounders known to be associated with perceived stress.[2] Adjusting tended to attenuate associations, but most outcome estimates remained significantly associated with the level of perceived stress. Some adjustment variables could be intermediate variables. Adjusting for them would underestimate the true association, but we chose this approach as it yields the most conservative estimates.[18]

Comparison with existing literature

To our knowledge, this is the first study to describe links between specific primary care services and level of stress as perceived by the patient. Existing evidence on the association between mental health and primary health care use is generally in line with our findings: psychosocial factors,[19] mental health problems,[20-22] and illness perception[23] was associated with frequent GP attendance even after accounting for the strong association between mental illness and physical health.[24-26] Multimorbidity is expected to increase the number of primary care consultations,[27-29] which is confirmed by our study.

Implications for research and practice

Stress appraisal was positively related to primary care activity level, regardless of mental and physical disease burden. However, the interpretation of appropriateness is difficult. A high level of perceived stress in itself does not justify a psychiatric diagnosis. As no official guidelines exist for non-syndromic stress in general practice, we cannot conclude whether the level of mental health related activities is appropriate. Interestingly, the treatment frequency was higher for antidepressants than for talk therapy provided by GPs or psychologist services. This tendency was stronger for persons with the highest stress levels and multimorbidity, especially three or more physical conditions. The underlying explanation for this association remains unknown, but persons with stress and physical multimorbidity may have a lower surplus of mental resources to interact in psychological treatment, or the complexity of health problems makes the GP decide to use the less resource-demanding pharmacological treatment. Yet, these treatment choices may be in contrast to the more general approach to mental health problems: Danish and international treatment guidelines recommend stepped care, where psychoeducation and psychosocial or psychological interventions are the first steps of choice before pharmacological treatment.[30,31]

High stress levels in patients with multimorbidity are associated with suboptimal care and adverse outcomes, e.g. more potentially preventable hospitalisations and high mortality.[2,4] Nevertheless, high stress levels were not associated with higher use of preventive chronic care services. This potential undertreatment or lack of timely chronic disease management in persons with mental-physical multimorbidity may play a role in the explanation of adverse outcomes. Conversely, highly stressed persons requested acute out-of-hours services more often than the less stressed, which is generally seen as a less desirable contact pattern for chronic disease management.[32]

The appropriate number of GP contacts and prescriptions for certain disease combinations cannot be deducted from our data because no information was available on the individual's full medical

complexity, self-efficacy, and social network. However, persons with high stress levels seemed to have a less timely appropriate use of primary care services. This, in addition to a poorer prognosis, calls for more focus on the mental well-being of patients even when no psychiatric illness is diagnosed. This also underlines the importance of the psychological aspect in the bio-psycho-social approach to treatment of persons with multimorbidity.

No validated clinical instrument is available for stress screening in general practice, and it is uncertain if screening is a good solution. Additionally, the GP may have a limited offer to patients with stress as no well-developed management guidelines exist. More importantly, the time frame and setting in which the GP meets the patient should support the assessment of the patient's mental well-being and resources. Patient-centred care is essential in achieving this goal.[33,34] Stress-alleviating interventions may improve the prognosis if the association between perceived stress and adverse outcomes is causal; mindfulness-based stress reduction could play a role.[35] Some evidence suggests that a collaborative and integrative approach may be beneficial in patients with mental-physical multimorbidity,[36,37] but more systematic research on stress and multimorbidity in primary care is needed.

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Ethical approval: The study was approved by the Danish Data Protection Agency (record number 2013-41-1719). All data were anonymized and securely stored at Statistics Denmark.

Competing interests: None declared.

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Data sharing statement: No additional data available.

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Tables and figures

Table 1. Study population characteristics according to Perceived Stress Scale quintile.

Characteristics	Total Number	Total Col %	PSS quintile 1 Row %	2 Row %	3 Row %	4 Row %	5 Row %
Median PSS score (range)			4 (0–6)	9 (7–10)	12 (11–13)	15 (14–17)	21 (18–40)
Age groups, years							
25-34	13,881	11.7	23.2	24.9	23.6	14.1	14.2
35-44	22,673	19.1	26.7	25.4	22.0	13.2	12.7
45-54	25,272	21.3	28.5	25.0	21.1	12.8	12.6
55-64	26,610	22.5	31.1	24.6	20.6	12.8	11.0
65-74	19,982	16.9	31.1	23.5	20.6	14.7	10.0
≥75	9,992	8.4	20.8	19.6	21.8	20.1	17.7
Sex							
Men	54,968	46.4	26.1	24.8	17.7	16.5	14.8
Women	63,442	53.6	19.4	22.3	18.1	19.0	21.2
Number of conditions							
0	58,718	49.6	25.6	26.3	18.9	16.5	12.7
1	2,5755	21.8	22.2	22.9	17.8	18.1	18.9
2	14,677	12.4	21.1	21.5	17.3	18.6	21.6
≥3	19,260	16.3	14.6	17.2	15.6	20.8	31.7
Any psychiatric condition							
No	109,137	92.2	23.8	24.6	18.4	17.7	15.5
Yes	9,273	7.8	7.3	10.9	12.3	19.5	50.0
Total	118,410	100.0	22.5	23.5	18.0	17.8	18.2

PSS: Perceived Stress Scale

Table 2. Cumulative incidence proportions and incidence rate ratios of mental health related primary care activities according to Perceived Stress Scale quintile.

Primary care service	PSS quintile	CIP_{1y}(%)	95% CI	IR	Crude IRR	Adj. IRR*	95% CI
Talk therapy by GP	1	1.1	(1.0,1.2)	0.02	1	1	Reference
	2	1.7	(1.5,1.8)	0.03	1.48	1.38	(1.15,1.65)
	3	2.2	(2.0,2.4)	0.04	2.01	1.72	(1.43,2.06)
	4	3.1	(2.9,3.3)	0.06	2.76	2.38	(1.99,2.83)
	5	6.8	(6.5,7.2)	0.15	6.90	4.96	(4.20,5.86)
Psychometric tests	1	1.2	(1.1,1.3)	0.02	1	1	Reference
	2	1.8	(1.6,1.9)	0.02	1.38	1.26	(1.06,1.51)
	3	2.5	(2.3,2.7)	0.04	2.04	1.75	(1.46,2.10)
	4	3.2	(2.9,3.4)	0.05	2.82	2.16	(1.82,2.56)
	5	6.6	(6.2,6.9)	0.10	5.96	3.68	(3.11,4.35)
Psychologist services	1	0.4	(0.4,0.5)	0.02	1	1	Reference
	2	0.7	(0.6,0.8)	0.04	1.57	1.49	(1.08,2.05)
	3	1.2	(1.0,1.3)	0.06	2.54	1.99	(1.47,2.69)
	4	1.5	(1.4,1.7)	0.08	3.53	3.07	(2.26,4.16)
	5	3.3	(3.1,3.6)	0.21	8.69	6.49	(4.90,8.58)
Psychiatrist services	1	0.2	(0.1,0.3)	0.01	1	1	Reference
	2	0.3	(0.3,0.4)	0.02	2.17	1.96	(1.16,3.32)
	3	0.5	(0.4,0.6)	0.03	3.20	1.92	(1.07,3.46)
	4	0.9	(0.8,1.0)	0.06	6.86	4.61	(2.77,7.69)
	5	3.7	(3.4,4.0)	0.24	28.74	13.26	(8.33,21.09)
Antidepressants prescriptions	1	2.6	(2.4,2.8)	0.10	1	1	Reference
	2	3.7	(3.5,3.9)	0.16	1.55	1.28	(1.09,1.49)
	3	5.7	(5.4,6.0)	0.25	2.37	1.84	(1.58,2.16)
	4	8.6	(8.2,9.0)	0.40	3.85	2.35	(2.04,2.71)
	5	21.5	(20.9,22.0)	1.21	11.63	4.62	(4.03,5.31)
Anxiolytics prescriptions	1	1.5	(1.4,1.7)	0.03	1	1	Reference
	2	2.0	(1.8,2.2)	0.05	1.61	1.53	(1.29,1.83)
	3	2.8	(2.6,3.0)	0.08	2.59	2.02	(1.67,2.44)
	4	4.1	(3.8,4.4)	0.13	4.27	2.56	(2.16,3.03)
	5	9.4	(9.0,9.8)	0.46	14.52	4.73	(4.03,5.54)
Hypnotics prescriptions	1	3.4	(3.2,3.6)	0.08	1	1	Reference
	2	4.3	(4.0,4.5)	0.11	1.39	1.34	(1.18,1.51)
	3	5.3	(5.0,5.6)	0.16	2.03	1.67	(1.47,1.89)
	4	6.6	(6.3,7.0)	0.22	2.77	1.83	(1.61,2.07)
	5	11.0	(10.6,11.5)	0.5	6.32	2.93	(2.59,3.31)

PSS: Perceived Stress Scale. CI: Confidence interval. CIP_{1y}: Cumulative incidence proportion at one year (in %). IR: Incidence rate. IRR: Incidence rate ratio.

*: adjusted for sex, age as 10-year age bands, presence of each of the 39 psychiatric and physical conditions in the multimorbidity index, socioeconomic factors, and lifestyle on index date.

Table 3. Cumulative incidence proportions and incidence rate ratios of general primary care and chronic care services according to Perceived Stress Scale quintile.

Primary care service	PSS quintile	CIP_{1y}(%)	95% CI	IR	Crude IRR	Adj. IRR*	95% CI
Spirometries	1	2.6	(2.4,2.8)	0.03	1	1	Reference
	2	3.0	(2.8,3.2)	0.04	1.15	1.12	(1.00,1.25)
	3	3.0	(2.8,3.3)	0.04	1.14	1.06	(0.94,1.19)
	4	3.6	(3.4,3.9)	0.05	1.40	1.17	(1.04,1.32)
	5	4.4	(4.1,4.6)	0.06	1.67	1.16	(1.03,1.31)
Blood sugar measures	1	13.9	(13.5,14.3)	0.21	1	1	Reference
	2	13.7	(13.3,14.1)	0.21	1.02	1.02	(0.97,1.07)
	3	14.7	(14.2,15.2)	0.23	1.08	1.05	(0.99,1.10)
	4	16.3	(15.8,16.8)	0.27	1.26	1.09	(1.04,1.15)
	5	18.4	(17.8,18.9)	0.3	1.44	1.12	(1.06,1.18)
ECGs	1	7.4	(7.1,7.7)	0.08	1	1	Reference
	2	7.7	(7.4,8.0)	0.09	1.03	1.05	(0.99,1.12)
	3	8.0	(7.6,8.4)	0.09	1.10	1.08	(1.02,1.16)
	4	9.2	(8.9,9.6)	0.11	1.29	1.17	(1.09,1.25)
	5	9.6	(9.3,10.1)	0.11	1.32	1.14	(1.07,1.22)
Home blood pressure measures	1	5.2	(4.9,5.5)	0.07	1	1	Reference
	2	5.2	(5.0,5.5)	0.07	0.99	1.05	(0.96,1.14)
	3	5.3	(5.0,5.6)	0.07	1.01	1.04	(0.95,1.14)
	4	5.6	(5.3,6.0)	0.08	1.11	1.10	(1.00,1.20)
	5	5.2	(4.9,5.5)	0.07	0.97	1.02	(0.93,1.13)
Annual chronic care consultations	1	18.1	(17.6,18.5)	0.31	1	1	Reference
	2	17.9	(17.5,18.4)	0.31	1.01	1.02	(0.97,1.06)
	3	18.7	(18.2,19.2)	0.33	1.09	1.04	(0.99,1.10)
	4	21.0	(20.4,21.5)	0.39	1.27	1.09	(1.04,1.14)
	5	23.8	(23.2,24.4)	0.47	1.53	1.22	(1.16,1.29)
Out-of-hours contacts	1	14.2	(13.8,14.7)	0.21	1	1	Reference
	2	16.1	(15.7,16.5)	0.25	1.16	1.07	(1.02,1.13)
	3	17.4	(16.9,18.0)	0.28	1.32	1.13	(1.07,1.19)
	4	19.7	(19.1,20.2)	0.33	1.57	1.22	(1.16,1.29)
	5	26.1	(25.6,26.7)	0.54	2.57	1.47	(1.39,1.55)
Daytime consultations	1	77.4	(76.9,77.9)	3.22	1	1	Reference
	2	79.9	(79.4,80.4)	3.46	1.07	1.04	(1.02,1.06)
	3	82.1	(81.6,82.6)	3.82	1.18	1.10	(1.07,1.12)
	4	84.7	(84.2,85.2)	4.45	1.38	1.18	(1.16,1.20)
	5	88.7	(88.3,89.2)	5.5	1.71	1.28	(1.25,1.30)

PSS: Perceived Stress Scale. CI: Confidence interval. CIP_{1y}: Cumulative incidence proportion at one year (in %). IR: Incidence rate. IRR: Incidence rate ratio.

*: adjusted for sex, age as 10-year age bands, presence of each of the 39 psychiatric and physical conditions in the multimorbidity index, socioeconomic factors, and lifestyle on index date.

Figure 1. Cumulative incidence proportions and incidence rate ratios of mental health related primary care services according to Perceived Stress Scale quintile and number of physical conditions.

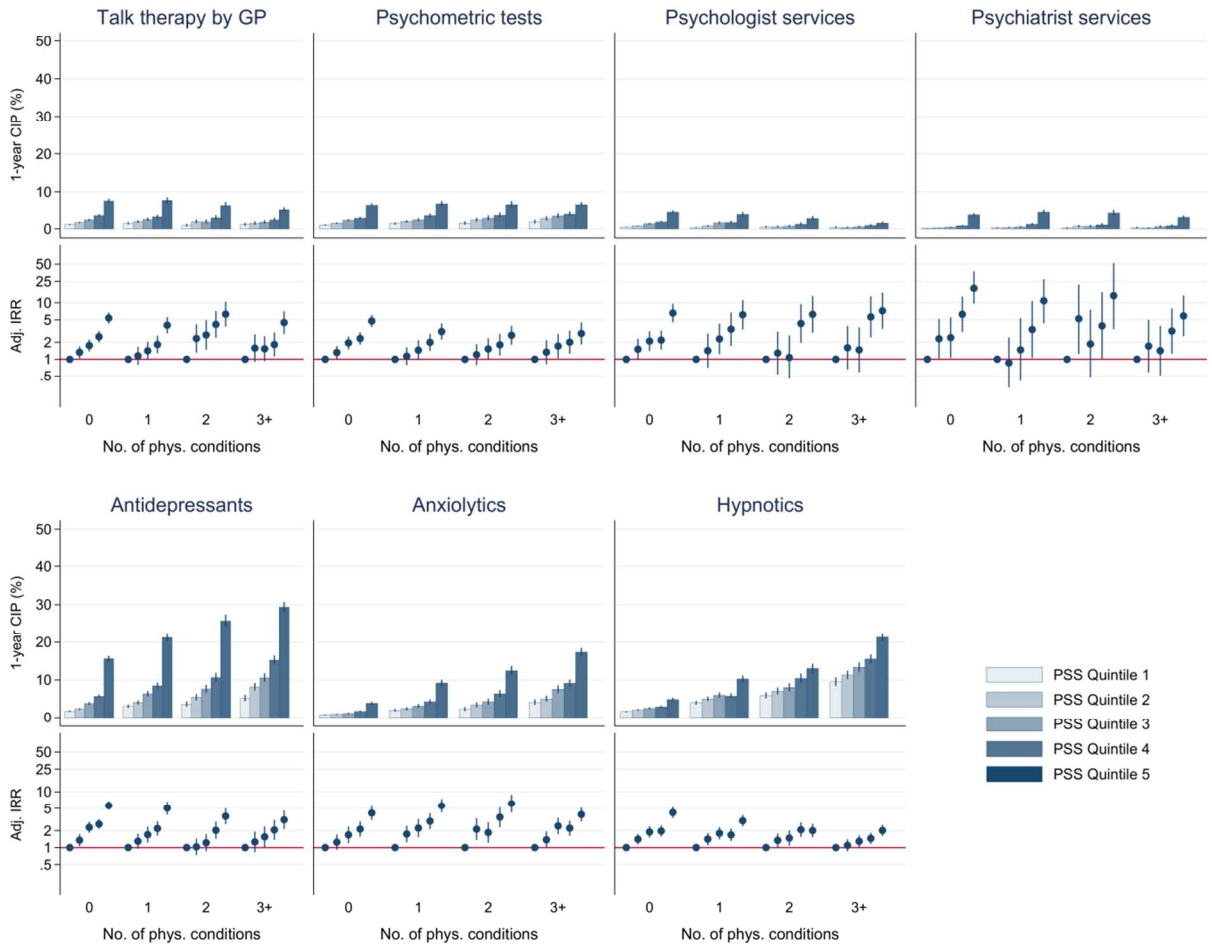
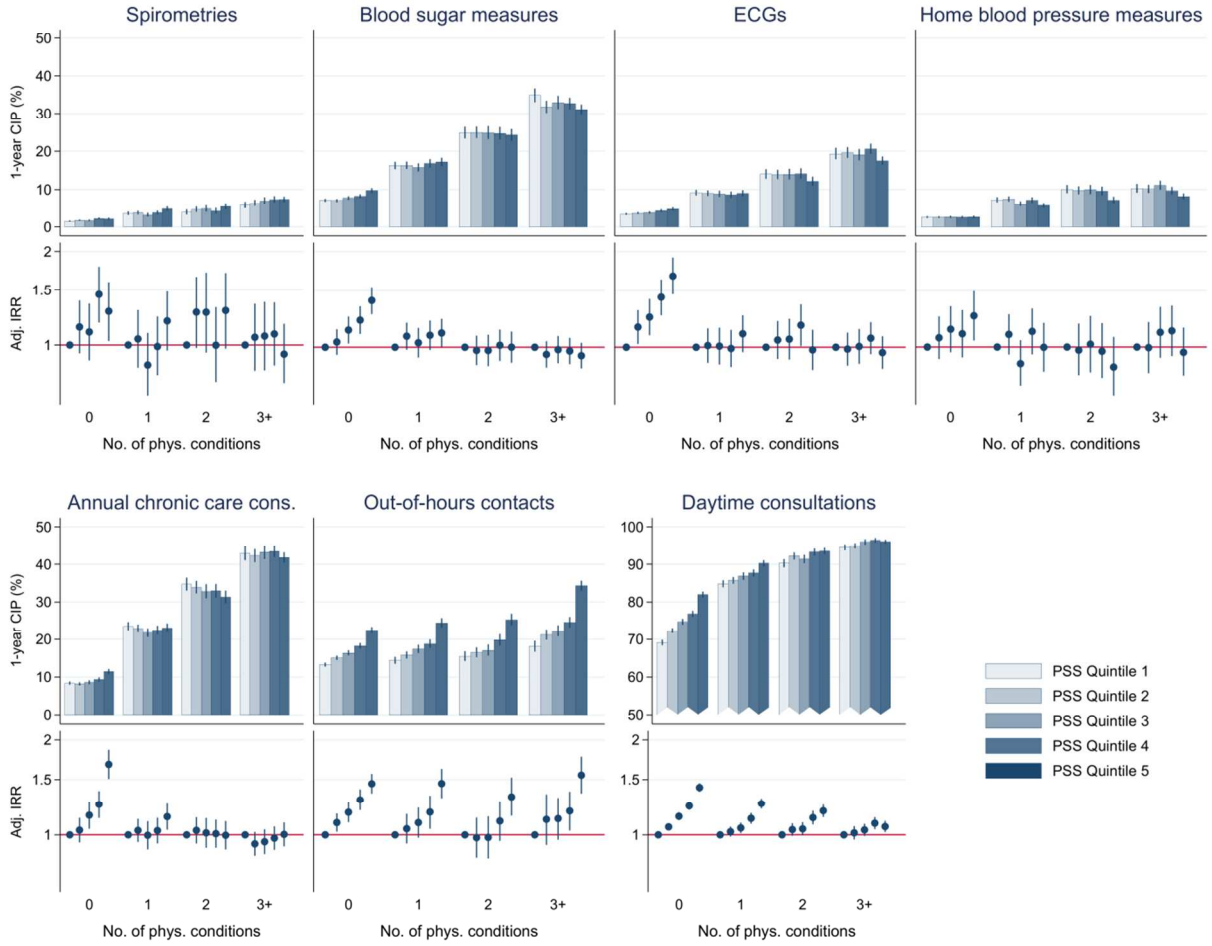
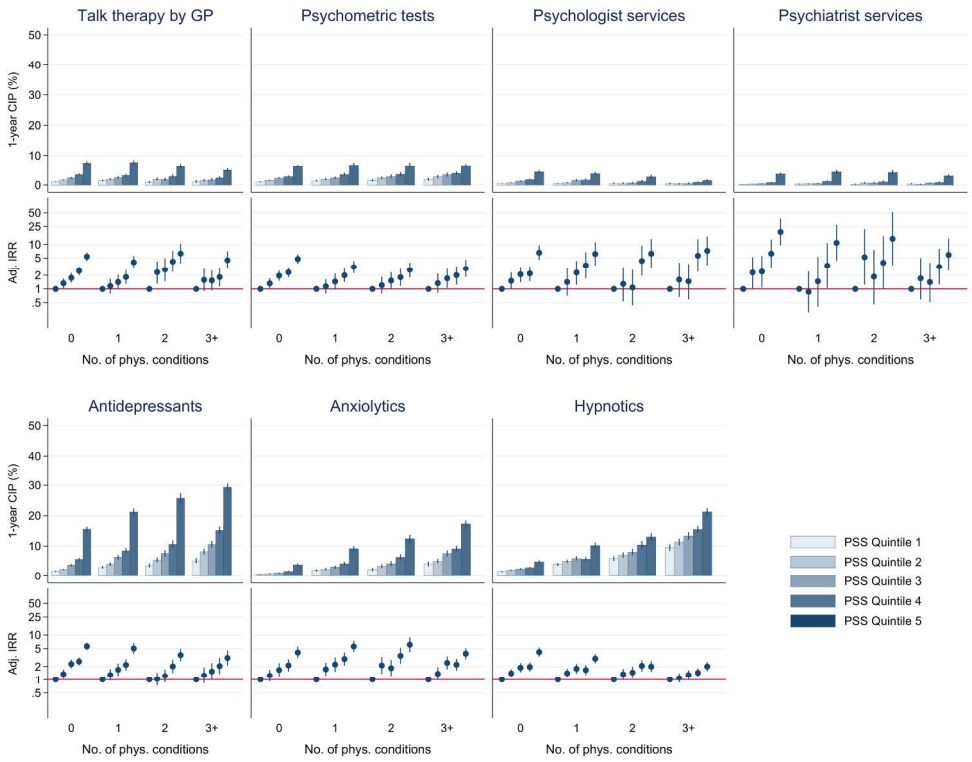


Figure 2. Cumulative incidence proportions and incidence rate ratios of general primary care and chronic care services according to Perceived Stress Scale quintile and number of physical conditions.





Cumulative incidence proportions and incidence rate ratios of mental health related primary care services according to Perceived Stress Scale quintile and number of physical conditions.

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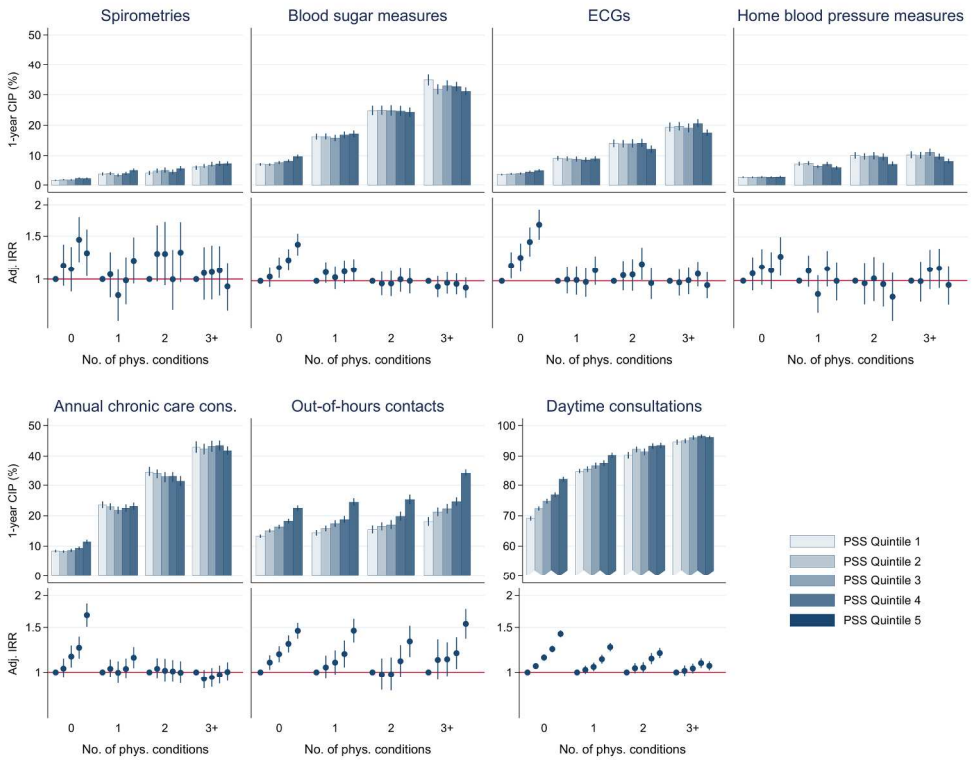

Cumulative incidence proportions and incidence rate ratios of general primary care and chronic care services according to Perceived Stress Scale quintile and number of physical conditions.

228x187mm (300 x 300 DPI)

Supplemental file

Perceived stress, multimorbidity, and use of primary care health services

eTable 1. Multimorbidity index diseases

Category	Disease group
Circulatory system	Hypertension
	Dyslipidemia
	Ischemic heart disease
	Atrial fibrillation
	Heart failure
	Peripheral artery occlusive disease
	Stroke
Endocrine system	Diabetes mellitus
	Thyroid disorder
	Gout
Pulmonary system and allergy	Chronic pulmonary disease
	Allergy
Gastrointestinal system	Ulcer/chronic gastritis
	Chronic liver disease
	Inflammatory bowel disease
	Diverticular disease of intestine
Urogenital system	Chronic kidney disease
	Prostate disorders
Musculoskeletal system	Connective tissue disorders
	Osteoporosis
	Painful condition
Haematological system	Anaemias
	HIV/AIDS
Cancers	Cancer
Neurological system	Vision problem
	Hearing problem
	Migraine
	Epilepsy
	Parkinson's disease
	Multiple sclerosis
	Neuropathies
Mental health conditions	Mood, stress-related, or anxiety disorders
	Psychological distress
	Alcohol problems
	Substance abuse
	Anorexia/bulimia
	Bipolar affective disorder
	Schizophrenia or schizoaffective disorder
	Dementia

HIV: human immunodeficiency virus; AIDS: acquired immunodeficiency syndrome.

[a]For details and coding definitions, please see Prior A, Fenger-Grøn M, Larsen KK, et al. The association between perceived stress and mortality among people with multimorbidity: A prospective population-based cohort study. Am J Epidemiol 2016;184:199-210.

eTable 2. Classification codes for services and prescriptions

Outcome	Danish National Health Service Register service codes*	ATC prescription codes
Talk therapy by GP	4003, 4021-4027, 4050, 4063, 4106, 4247-4249, 6101 (daytime)	
Psychometric tests	2149 (daytime)	
Psychologist services	0100-0299, 1000-3999 (daytime)	
Psychiatrist services	0110-0140, 0210-0236 (daytime)	
Antidepressant prescriptions		N06AB, N06AF, N06AG, N06AX (N06AX12 & N06AX05 excluded)
Anxiolytics prescriptions		N05BA, N05BE
Hypnotics prescriptions		N05CD, N05CF, N05CH
Daytime consultations	0101 (daytime)	
Out-of-hours contacts (telephone, consultations, home visits)	0501, 0602, 04XX (out-of-hours)	
Annual chronic care consultations	0106, 0120 (daytime)	
Spirometries	7113 (daytime)	
Blood sugar measures	7136 (daytime)	
ECGs	7156 (daytime)	
Home blood pressure measures	2146 (daytime)	

ATC: Anatomical Therapeutic Chemical classification.
* Provider specialty is general practice (codes 80-89), except for psychologists services (code 63) and psychiatrist services (code 24).

eTable 3. Incidence rate ratios of primary care services according to Perceived Stress Scale quintile for persons without psychiatric illness (N=109,137)

Activity	PSS quintile	Adj. IRR*	95% CI	Activity	PSS quintile	Adj. IRR*	95% CI
Talk therapy by GP	1	1	Reference	Spirometries	1	1	Reference
	2	1.36	(1.12,1.66)		2	1.10	(0.98,1.24)
	3	1.61	(1.32,1.96)		3	1.07	(0.94,1.21)
	4	2.39	(1.98,2.89)		4	1.15	(1.01,1.30)
	5	5.22	(4.36,6.26)		5	1.16	(1.01,1.32)
Psychometric tests	1	1	Reference	Blood sugar measures	1	1	Reference
	2	1.26	(1.05,1.52)		2	1.03	(0.98,1.08)
	3	1.78	(1.47,2.16)		3	1.06	(1.00,1.11)
	4	2.14	(1.78,2.58)		4	1.09	(1.04,1.16)
	5	3.99	(3.33,4.78)		5	1.12	(1.06,1.19)
Psychologist services	1	1	Reference	ECGs	1	1	Reference
	2	1.53	(1.09,2.15)		2	1.05	(0.99,1.12)
	3	1.97	(1.43,2.72)		3	1.08	(1.01,1.16)
	4	3.05	(2.21,4.23)		4	1.16	(1.09,1.24)
	5	6.83	(5.05,9.23)		5	1.15	(1.07,1.24)
Psychiatrist services	1	1	Reference	Home blood pressure measures	1	1	Reference
	2	2.17	(1.12,4.19)		2	1.06	(0.97,1.15)
	3	2.32	(1.14,4.71)		3	1.04	(0.95,1.14)
	4	5.69	(3.08,10.52)		4	1.09	(1.00,1.20)
	5	25.45	(14.54,44.54)		5	1.04	(0.93,1.15)
Antidepressants prescriptions	1	1	Reference	Annual chronic care consultation	1	1	Reference
	2	1.30	(1.04,1.63)		2	1.03	(0.98,1.07)
	3	2.22	(1.78,2.76)		3	1.05	(1.00,1.11)
	4	2.84	(2.31,3.50)		4	1.09	(1.04,1.15)
	5	6.79	(5.59,8.25)		5	1.24	(1.17,1.31)
Anxiolytics prescriptions	1	1	Reference	Out-of-hours contacts	1	1	Reference
	2	1.54	(1.27,1.87)		2	1.07	(1.01,1.13)
	3	2.07	(1.69,2.55)		3	1.13	(1.07,1.19)
	4	2.67	(2.21,3.24)		4	1.23	(1.16,1.30)
	5	5.01	(4.18,6.00)		5	1.47	(1.39,1.55)
Hypnotics prescriptions	1	1	Reference	Daytime consultations	1	1	Reference
	2	1.33	(1.17,1.51)		2	1.04	(1.02,1.06)
	3	1.61	(1.41,1.84)		3	1.09	(1.07,1.12)
	4	1.86	(1.63,2.12)		4	1.17	(1.14,1.19)
	5	2.96	(2.59,3.38)		5	1.28	(1.25,1.31)

PSS: Perceived Stress Scale. IRR: Incidence rate ratio.

*: adjusted for sex, age as 10-year age bands, presence of each of the 39 psychiatric and physical conditions in the multimorbidity index, socioeconomic factors, and lifestyle on index date.

eTable 4. Incidence rate ratios for primary care activities requested by non-respondents versus respondents

Activity	Non-respondent crude IRR	95% CI	Non-respondent adjusted IRR*	95% CI
Talk therapy by GP	1.18	(1.11,1.25)	1.23	(1.15,1.31)
Psychometric tests	1.20	(1.13,1.27)	1.14	(1.07,1.22)
Psychologist services	0.93	(0.85,1.02)	0.95	(0.83,1.09)
Psychiatrist services	1.32	(1.20,1.46)	1.46	(1.23,1.73)
Antidepressant prescriptions	1.96	(1.88,2.03)	1.46	(1.37,1.56)
Anxiolytics prescriptions	2.34	(2.20,2.48)	1.93	(1.78,2.09)
Hypnotics prescriptions	1.70	(1.62,1.79)	1.38	(1.30,1.47)
Spirometries	0.86	(0.81,0.91)	0.94	(0.88,0.99)
Blood sugar measures	0.94	(0.91,0.96)	0.97	(0.95,1.00)
ECGs	0.82	(0.79,0.85)	0.88	(0.86,0.91)
Home blood pressure measures	0.74	(0.70,0.77)	0.88	(0.84,0.93)
Annual chronic care consultation	0.88	(0.86,0.90)	0.93	(0.91,0.96)
Out-of-hours contacts	1.59	(1.51,1.68)	1.20	(1.17,1.23)
Daytime consultations	0.94	(0.93,0.95)	0.95	(0.94,0.96)

IRR: Incidence rate ratios.
*: IRRs adjusted for sex, age as 10-year age bands, presence of each of the 39 psychiatric and physical conditions in the multimorbidity index, cohabitation status, and educational level on index date.
The reference for each activity is survey respondents.

eTable 5. Incidence rate ratios for general primary care services in persons with any psychiatric condition versus persons without psychiatric conditions according to survey response status

		Respondents		Non-respondents	
Activity	Any psychiatric condition	Adj. IRR	95% CI	Adj. IRR	95% CI
Annual chronic care consultation	No	1	Reference	1	Reference
	Yes	1.39	(1.15,1.68)	1.26	(1.04,1.53)
Out-of-hours contacts	No	1	Reference	1	Reference
	Yes	1.77	(1.43,2.18)	1.85	(1.50,2.28)
Daytime consultations	No	1	Reference	1	Reference
	Yes	1.35	(1.24,1.48)	1.33	(1.21,1.45)

IRR: Incidence rate ratios.

*: IRRs adjusted for sex, age as 10-year age bands, presence of each of the 39 psychiatric and physical conditions in the multimorbidity index, cohabitation status and educational level on index date.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Described on page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1–2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2–3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5–7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5–6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5–7, eTable 1 eTable 2
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6–7, eTable 1 eTable 2
Bias	9	Describe any efforts to address potential sources of bias	7–8
Study size	10	Explain how the study size was arrived at	5–6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6–8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	8
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods	6–8

		taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5, 8
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8, 9, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	9
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	8 Table 2–3
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8, 9, Table 2–3
		(*b*) Report category boundaries when continuous variables were categorized	Table 1
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Table 2–3
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10, Figure 1–2 eTable 3, eTable 4, eTable 5
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11–12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12–14
Generalisability	21	Discuss the generalisability (external validity) of the study results	11, 13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at

http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

The association between perceived stress, multimorbidity, and primary care health services – a Danish population-based cohort study

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The association between perceived stress, multimorbidity, and primary care health services – a Danish population-based cohort study

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Abstract

Objectives

Mental stress is common in the general population. Mounting evidence suggests that mental stress is associated with multimorbidity, suboptimal care, and increased mortality. Delivering healthcare in a bio-psycho-social context is key for general practitioners (GPs), but it remains unclear how persons with high levels of perceived stress are managed in primary care. We aimed to describe the association between perceived stress and primary care services by focussing on mental health related activities and markers of elective/acute care while accounting for mental-physical multimorbidity.

Design

Population-based cohort study.

Setting

Primary healthcare in Denmark.

Participants

118,410 participants from the Danish National Health Survey 2010 followed for one year. Information on perceived stress and lifestyle was obtained from a survey questionnaire. Information on multimorbidity was obtained from health registers.

Outcome measures

General daytime consultations, out-of-hours services, mental health related services, and chronic care services in primary care obtained from health registers.

Results

Perceived stress levels were associated with primary care activity in a dose-response relation when adjusted for underlying conditions, lifestyle, and socioeconomic factors. In the highest stress quintile, 6.8% attended GP talk therapy (highest versus lowest quintile, adjusted incidence rate ratios (IRR): 4.96, 95% CI: 4.20–5.86), 3.3% consulted a psychologist (IRR: 6.49, 95% CI: 4.90–8.58), 21.5% redeemed an

antidepressant prescription (IRR: 4.62, 95% CI: 4.03–5.31), 23.8% attended annual chronic care consultations (IRR: 1.22, 95% CI: 1.16–1.29), and 26.1% used out-of-hours services (IRR: 1.47, 95% CI: 1.51–1.68). For those with multimorbidity, stress was associated with more out-of-hours services, but not with more chronic care services.

Conclusion

Persons with high stress levels generally had higher use of primary healthcare, 4–6 times higher use of mental health related services (most often in the form of psychotropic drug prescriptions), but less timely use of chronic care services.

Keywords (MeSH): stress, psychological; practice patterns, physicians'; primary health care; family practice; general practice; comorbidity

Article summary

Strengths and limitations of this study

- This is the first population-based cohort study to investigate the association between stress perception and primary healthcare utilization while taking multimorbidity into account.
- A major strength of the study was the large cohort of 118,410 participants in the Danish National Health Survey 2010 who answered questions on stress, lifestyle and socioeconomic factors.
- The participants' self-reported data were linked at the individual level with national health register information on multimorbidity status, vital status, and primary care daytime and out-of-hours services, which ensured virtually no loss to follow-up.
- Multimorbidity was assessed by prospectively recorded register-based data on diagnoses and medication prescriptions for 39 mental and physical conditions.
- The limitations of this study include the lack of data on stress in non-respondents, the lack of data on private practicing psychologists, and no access to primary care medical records with details on the provided services and diagnoses.

Introduction

Mental stress that does not fulfil the criteria for any psychiatric disorder is common in the population.[1,2] This type of mental stress has gained increasing attention because of the emerging evidence on its impact on the physical health; stress is highly associated with disease burden and physical multimorbidity (i.e. two or more conditions in the same individual).[1-5] Persons with high stress levels have a poor prognosis of physical disease, e.g. cardiovascular events and metabolic syndrome.[6-8] Increased mortality rates are also seen,[9] even after adjusting for mental-physical multimorbidity.[2,10] Allostatic load theory constitutes a theoretical framework for physiological pathways that may explain these well-documented relations between mental and physical well-being.[11,12]

Mental health problems (including stress) and multimorbidity have been linked to high – and potentially inappropriate – healthcare utilization. This includes emergency contacts, unplanned admissions, and potentially preventable hospitalisations.[13-20] High perceived stress levels are inversely related to self-efficacy, which may affect the development of chronic conditions.[21] Mental stress is an increasingly common reason for contacting the general practitioner (GP),[22] but little is known about the services provided by GPs and other health professionals in primary care to persons with high levels of stress. In line with Anderson's behavioural model of healthcare utilization,[23] we hypothesised that high levels of perceived stress as a predisposing factor would increase the overall number of contacts to the GP, specifically the number of contacts related to mental health. We also hypothesised that the provided care would differ depending on the burden of mental and physical comorbidities. Mental symptoms may overshadow physical symptoms, and this may prevent adequate chronic care.[24-26] High levels of perceived stress was thus hypothesised to be associated with poorer chronic care in those with multimorbidity.

We aimed to describe the association between the perceived stress level in the patients and the overall frequency of day-time and out-of-hours contacts, chronic care contacts, and mental health related contacts in primary care while taking into account multimorbidity as a potential confounder and a moderator of the stress effects.

Methods

Study population, design and setting

The study population consisted of respondents (age > 25 years) from the nationwide Danish National Health Survey of 2010.[27] Survey questionnaires were collected by 1 May 2010 (index date). We excluded persons who died or emigrated before this date (2,235 persons). A total of 118,410 (response rate: 56%) returned the questionnaire with information on all perceived stress items.

We conducted a population-based cohort study with up to one year of follow-up until death, emigration, or end-of-study (1 May 2011), whichever came first. Using the personal identification number assigned to all Danish citizens,[28] we linked individual-level data across survey responses and health registers. Almost all Danish citizens are listed with a GP providing them with universal tax-funded access to healthcare.[29] The GP acts as a gatekeeper to secondary care and may refer to other publicly funded services in primary care.[30] Referrals to private practicing psychiatrists are fully covered by the healthcare system. Referrals to psychologists are partly covered if certain criteria are fulfilled, e.g. a diagnosis of depression or anxiety, or loss of a first-degree relative, but not high perceived stress in itself.

Danish GPs are contractors in a partly per capita, partly fee-for-service remuneration system.[31] The contract with the public healthcare system defines reimbursement fees for daytime consultations and out-of-hours services (typically from 4 pm to 8 am). Most medical work is covered by an unspecific base

fee, but some specific services performed during the consultation, e.g. talk therapy or psychometric testing, are additionally reimbursed. Annual chronic care consultations can be performed once a year for each chronic condition and are remunerated by a special fee. Invoices from the contractors are recorded in the Danish National Health Service Register, which provided us with data on all contacts and publicly reimbursed services performed by Danish GPs, psychologists, and psychiatrists.[32]

Drug prescriptions are not recorded in the Danish National Health Service Register, but the Danish National Prescription Registry provided data on redeemed drug prescriptions based on data from all Danish pharmacies.[33]

Perceived stress

In the survey questionnaire, we measured perceived stress by Cohen's Perceived Stress Scale (PSS).[34-36] The PSS has been widely used and psychometrically validated as a reliable measure of psychological stress.[35,36] It is based on a five-level Likert-style questionnaire with items on general stress, coping, and feeling of control. The 10-item Danish version produces a sum score of 0–40; 40 points represent the highest perceived stress level. The PSS has no predefined cut-off values,[34] but fifth quintile values are often considered abnormal.[1] The stress score was, therefore, divided into quintiles to assess potential non-linear relations with outcomes.

Multimorbidity

The health status of each participant on the index date was assessed using a multimorbidity index of eight psychiatric and 31 physical long-term conditions (eTable 1) identified in Danish nationwide health registers by a previously described algorithm.[2] The algorithm combined data on diagnoses from all

Danish hospitals and out-patient clinics with redeemed drug prescriptions from all Danish pharmacies. This approach is in line with recognised international measures of multimorbidity.[37] No international consensus on the choice of multimorbidity indices exists, apart from some key diseases that are always included.[38,39] Multimorbidity was defined as two or more coexisting conditions.[40]

Outcomes

Our main outcomes of interest were selected from the list of reimbursed services and redeemed drug prescriptions. These were categorised into three groups: 1) services related to mental health (GP talk therapy, GP psychometric tests, and sessions with a publicly reimbursed private practicing psychologist or psychiatrist) and redemption of psychotropic medication, 2) services in general practice related to elective chronic care (spirometry test for lung disease, blood sugar sampling for diabetes, electrocardiograms (ECGs), home blood pressure monitoring for cardiovascular disease, and annual chronic care consultations [one annual review meeting per chronic disease per patient]), and 3) the overall rate of consultations based on the time of day, i.e. daytime face-to-face consultations with GPs and out-of-hours services (telephone or face-to-face consultations with GP).

The service codes and "Anatomical Therapeutic Chemical" (ATC) medication codes used to identify the outcomes can be found in the Appendix (eTable 2).

Other covariates

Information on the highest achieved education level according to the UNESCO classification system (<10 years, 10-15 years, >15 years of education),[41] cohabitation status (single or cohabiting), and ethnicity (Danish, other western background, other) was obtained from Statistics Denmark.[42] The Danish Civil

Registration System provided information on sex, age (10-year age bands), and vital status (alive, dead, or emigrated).[28] Information on working status (currently employed or unemployed, students, and retirees) and lifestyle factors (physical activity [light or no weekly activity, moderate activity ≥4 hours weekly, hard activity ≥4 hours weekly], body mass index [underweight < 18, normal weight 18-25, overweight 25-30, obese > 30], and alcohol [drinks per week for men and women], smoking [never smoker, former smoker, current smoker], and dietary habits [unhealthy, medium, healthy]) was obtained from the survey.

Statistical analysis

Cumulative incidence proportions (CIPs), which reflect the proportion of persons with at least one contact at one year after the index date, and incidence rates (IRs), which reflect the total number of contacts during follow-up were calculated for all investigated primary care activities. We used a negative binomial regression model to calculate incidence rate ratios (IRRs) by PSS score quintiles and assigned the first PSS quintile as the reference. We then adjusted for sex, age as 10-year age bands, and presence of each of the 39 conditions in the multimorbidity index, lifestyle factors, and socioeconomic factors on the index date. We included the time at risk to account for death or immigration in both models. Cluster robust variance estimation was used to estimate 95% confidence intervals (95% CIs) to account for inter-individual heterogeneity. We imputed missing data on lifestyle and socioeconomic factors in a chained equations model of all our analysis parameters and produced 20 imputation sets.[43] To assess the effect modification from disease burden, we stratified the analyses on the number of the 31 physical conditions of the multimorbidity index.

Three sensitivity analyses were performed to test the robustness of our results. Firstly, we included in our analysis only persons without diagnosed psychiatric illness to separate the effect of perceived stress

and symptoms related to psychiatric illness. Secondly, we performed a non-response analysis to test the generalisability of our findings; analyses of general primary care outcomes were carried out using register-based information on both survey respondents and non-respondents for which psychiatric illness acted as a proxy for stress (because the PSS score was unobtainable for non-respondents). Thirdly, a complete-case analysis, which excluded persons with missing data, was performed to validate the use of multiple imputations on missing values.

All analyses were performed using Stata 13.1 (StataCorp, College Station, TX).

The study was performed in accordance with the STROBE guidelines.

Results

The median age was 54 years (interquartile range: 23 years). The median PSS score was 11. Within the one year of follow-up, the study population was at risk for 117,856 person-years. A total of 1,042,353 reimbursed primary care services and 85,962 redeemed psychotropic prescriptions of interest were recorded. The perceived stress levels were generally higher for women and tended to increase with increasing number of physical conditions and presence of psychiatric morbidity (Table 1). The distribution of survey variables across PSS quintiles has been reported elsewhere.[2]

Perceived stress and primary care activities

For all primary care activities, except home blood pressure monitoring, a dose-response relation seemed to exist between the perceived stress level and the probability of receiving a primary care service or psychotropic prescription during follow-up (Tables 2 and 3, 1-year CIPs). The highest IRRs associated

with perceived stress were found for mental health related activities, but adjustments attenuated the association (Table 2, IRRs). Among the highest stress quintile, 6.8% attended GP talk therapy (highest versus lowest PSS quintile; adjusted IRR: 4.96, 95% CI: 4.20–5.86), 3.3% consulted a psychologist (IRR: 6.49, 95% CI: 4.90–8.58), 3.7% consulted a psychiatrist (IRR: 13.26, 95% CI: 8.33–21.09), 21.5% redeemed an antidepressant prescription (IRR: 4.62, 95% CI: 4.03–5.31), 23.8% attended annual chronic care consultations (IRR: 1.22, 95% CI: 1.16–1.29), and 26.1% used out-of-hours services (IRR: 1.47, 95% CI: 1.51–1.68). The proportion of persons who visited their GP at least once during the follow-up year rose with increasing stress levels from 77% to 89% (Table 3).

Perceived stress and primary care activities by multimorbidity level

The IRRs for receiving a mental health related service generally remained stable across PSS quintiles, regardless of underlying disease count (Figure 1, IRRs). However, in absolute terms, the use of talk therapy and psychologist services decreased and psychotropic drug prescriptions increased with increasing numbers of physical conditions (Figure 1, 1-year CIP).

Nearly all persons with physical multimorbidity visited their GP during the investigated year. Multimorbidity in itself was associated with use of elective chronic care services, i.e. annual chronic care consultations, blood sugar measures, ECGs, and home blood pressure monitoring (Figure 2). In those with multimorbidity, higher stress levels were not associated with more elective chronic care services than lower stress levels. In absolute numbers, the use of chronic care services tended to decrease with increasing stress level. Stress was generally associated with use of acute out-of-hours services, regardless of multimorbidity level, but those with multimorbidity tended to have higher use (Figure 2).

Sensitivity analyses

Excluding persons with psychiatric illness from the analyses did not change the overall pattern of primary care activities (eTable 3). The non-response analyses showed that survey non-respondents more often were men and mentally ill ($p<0.001$) and less often used daytime consultations and services related to chronic care (eTable 4). The adjusted IRRs of general primary care services were similar, regardless of response status when using psychiatric illness as a proxy for high levels of perceived stress (eTable 5). The complete case analysis showed virtually no differences from our main analysis with multiple imputed data (data not shown).

Discussion

Summary of findings

This population-based cohort study showed that the primary care activities increased with increasing perceived stress levels, even after adjusting for co-existing mental and physical conditions, lifestyle, and socioeconomic factors. However, in absolute numbers few persons with high levels of perceived stress used mental health services, and more persons received psychotropic medication prescriptions than talk therapy. The rate of preventive services, e.g. annual chronic care consultations and disease monitoring tests, did not increase with increasing stress levels in persons with multimorbidity. Most persons with high stress levels were in contact with their GP during the investigated year and had higher use of out-of-hours services than those with low stress levels.

Strengths and limitations

This study was based on unique information on stress levels and lifestyle factors in a large random sample of the Danish background population. The Danish Civil Registration System[28] allowed us to link information across healthcare registers and ensured no loss to follow-up.

Non-respondents tended to be different from survey respondents. Therefore, the absolute number of contacts to primary healthcare in our study may not be generalisable to the whole population. However, we have no reason to believe that response status affected the adjusted association between perceived stress and use of primary healthcare as the service use was similar among respondents and non-respondents using a proxy for stress.

Both definition and measurement of stress depend on the chosen recognised stress paradigm of which several exist. Stress can be seen as a fairly objective external factor and measured as the perceived magnitude and duration of a specific stressor, such as a stressful life event or long-term work stress exposure.[44] Another approach is to assess stress through stress hormone levels and physiological responses to stress in the body.[11] In this study, we approached mental stress as a subjective self-reported state reflecting the balance between perceived stressful events and individual coping mechanisms.[45] This paradigm recognises that adaptation to stress is subject to numerous individual factors, including genetic predisposition and social context. The allostatic load theory synthesises the above mentioned stress paradigms in a theoretical framework focusing on the dynamic adaptation to stress over time.[46] Assessing perceived stress through a survey at one point in time has an important limitation; we do not know for how long the observed stress level has been present, but the PSS seems to remain fairly stable over time.[47]

Danish health register data are prospectively recorded and validated; these data are considered to be of high quality.[28,32,33] All GPs report their patients' service use, and all pharmacies report redeemed prescriptions.[29] As reporting of primary care services is economically incentivised, high completeness is

expected.[32] Reporting may be incomplete if the GP forgets to register a service (e.g. talk therapy). However, the GP's reporting is probably unaffected by patient stress levels; a potential misclassification is thus non-differential. Patients with more severe or complicated chronic disease may be followed in outpatient clinics and have fewer GP chronic care visits. If stress level was a marker of disease severity, this may explain the lack of association between stress and chronic care services among persons with multimorbidity. Psychologist services are probably well recorded in the health registers for reimbursement purposes, whereas visits paid by e.g. insurance companies and municipal or private organisations are not; the use of psychologists may hence be underestimated in our study.

Multimorbidity status was assessed at the time of the survey by using an algorithm of prospectively collected register data for up to 15 years before baseline.[2] The lack of a Danish register for primary care diagnoses meant that multimorbidity status was based on outpatient and hospital discharge diagnoses combined with recordings of repeated prescriptions. This provided us with information on chronic conditions that were commonly managed in primary care, but the capture may not be complete.[2] Psychiatric diagnoses were based on contacts to the psychiatric hospitals and out-patient clinics combined with prescriptions of psychotropic drugs; there may be a general under-recognition of psychiatric conditions in primary care, and the distinction between e.g. stress and depression may vary among GPs.[48]

The combined data sources from the survey and registers allowed us to adjust for demographic, lifestyle, and socioeconomic confounders that are known to be associated with perceived stress.[2] Adjusting tended to attenuate associations, but most outcome estimates remained significantly associated with the level of perceived stress. Some adjustment variables could be intermediate variables. Adjusting for them would underestimate the true association, but we chose this approach as it yields the most conservative estimates.[49]

For this type of epidemiological study, we lacked detailed GP records data to examine the context of the treatment and to conclude which specific factors in the patient, the doctor, and the healthcare system are most likely to cause the observed findings.

Comparison with existing literature

To our knowledge, this is the first study to describe links between specific primary care services and level of stress as perceived by the patient. Existing evidence on the association between mental health and primary healthcare use is generally in line with our findings: psychosocial factors,[50] mental health problems,[51-53] and illness perception[54] are associated with frequent GP attendance even after accounting for the strong association between mental illness and physical health.[55-57] Multimorbidity is expected to increase both the number of primary care consultations and the general prescription rate,[58-60] which is also confirmed by our study. The effect of multimorbidity on healthcare consumption may be modified by personal factors that are known to be associated with appraised stress level, e.g. gender, age, and continuity of care.[61]

The finding that stress may lead to less timely chronic care is supported by the literature on mental-physical multimorbidity; a combination of psychiatric and physical conditions seems to hinder sufficient consultation time, impose errors, and impair the general quality of chronic care in primary care.[62,63] High utilization of out-of-hours services and unscheduled care have been described in patients with mental health problems including stress,[20] specifically in patients with chronic conditions, although disease burden or severity may confound the association.[19,64] In our study, we had the statistical power to take into account the confounding factor of multimorbidity to counter this.

Implications for research and practice

Stress appraisal was positively related to primary care activity level, regardless of mental and physical disease burden. However, the interpretation of appropriateness is difficult. A high level of perceived stress in itself does not justify a psychiatric diagnosis. As no official guidelines exist for non-syndromic stress in general practice, we cannot conclude whether the level of mental health related activities is appropriate. Interestingly, the treatment frequency was higher for antidepressants than for talk therapy provided by GPs or psychologist services. This tendency was stronger for persons with the highest stress levels and multimorbidity, especially three or more physical conditions. The underlying explanation for this association remains unknown, but persons with stress and physical multimorbidity may have a lower surplus of mental resources to interact in psychological treatment, or the complexity of health problems makes the GP decide to use the less resource-demanding pharmacological treatment. Yet, these treatment choices may be in contrast to the more general approach to mental health problems: Danish and international treatment guidelines recommend stepped care, where psychoeducation and psychosocial or psychological interventions are the first steps of choice before pharmacological treatment.[65,66] However, we had no means to assess the exact treatment history and the duration of the appraised level of stress in this study. Therefore, patients with multimorbidity may already have tried a number of treatment options if they have had stress for a longer period of time.

In the literature, high stress levels in patients with multimorbidity are associated with suboptimal care and adverse outcomes, e.g. more potentially preventable hospitalisations and high mortality.[2,18] In our study, high stress levels were not associated with higher use of preventive chronic care services for those with severe multimorbidity; more chronic care services than observed would be expected and considered appropriate in those with high stress levels. This potential undertreatment or lack of timely chronic disease management in persons with mental-physical multimorbidity may play a role in the

explanation of adverse outcomes. Conversely, highly stressed persons requested acute out-of-hours services more often than the less stressed, which is generally seen as a less desirable contact pattern for chronic disease management.[67]

The appropriate number of GP contacts and prescriptions for certain disease combinations cannot be deducted from our data because no information was available on the individual's full medical complexity, self-efficacy, and social network. However, persons with high stress levels seemed to have a less timely appropriate use of primary care services. This, in addition to a poorer prognosis, calls for more focus on the mental well-being of patients even when no psychiatric illness is diagnosed. This also underlines the importance of the psychological aspect in the bio-psycho-social approach to treatment of persons with multimorbidity.

The PSS measures an independent stress construct and was originally intended as a one-dimensional scale without predefined cut-off values.[34] The value of the score may not be easily interpretable in a clinical setting, and caseness is difficult to operationalise. Stress symptoms are common in psychiatric disorders and overlaps exist, which is also reflected in the correlation between measurements of stress, depression, and anxiety.[36,68,69] However, directing the focus away from diagnoses has important strengths, e.g. less stigmatization and reduced focus on pharmacological treatment. No validated clinical instrument is available for stress screening in general practice, and it is uncertain if screening is a good solution. Additionally, the GP may not be able to offer patients with stress much treatment as no well-developed management guidelines exist. More importantly, the time frame and setting in which the GP meets the patient should support the assessment of the patient's mental well-being and resources. This can be challenging for the GPs in patients with multimorbidity, where the treatment is multifaceted, and care is strongly affected by psychosocial factors.[70] Models of collaborative and integrated care aim to redefine the GP consultation and focus more on empowering patients with co-existing mental and

physical health problems.[71,72] Patient-centred care is essential in achieving this goal.[73,74] Stress-alleviating interventions may improve the prognosis if the association between perceived stress and adverse outcomes is causal. Mindfulness-based stress reduction and problem-solving therapy could play a role.[75,76]

Mental stress and multimorbidity are common problems that often coexist in the general population. Therefore, even a small impact of stress on the prognosis and general healthcare utilization may be relevant in public health. Future research should explore potential management strategies and preventive interventions aimed at patients with mental stress. Patient-centred care research and qualitative research conducted in primary care may provide some new answers to these questions.

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Ethical approval: The study was approved by the Danish Data Protection Agency (record number 2013-41-1719). All data were anonymized and securely stored at Statistics Denmark.

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Tables and figures legends

Table 1. Study population characteristics according to Perceived Stress Scale quintile.

Characteristics	Total Number	Total Col %	PSS quintile 1 Row %	2 Row %	3 Row %	4 Row %	5 Row %
Median PSS score (range)			4 (0–6)	9 (7–10)	12 (11–13)	15 (14–17)	21 (18–40)
Age groups, years							
25-34	13,881	11.7	23.2	24.9	23.6	14.1	14.2
35-44	22,673	19.1	26.7	25.4	22.0	13.2	12.7
45-54	25,272	21.3	28.5	25.0	21.1	12.8	12.6
55-64	26,610	22.5	31.1	24.6	20.6	12.8	11.0
65-74	19,982	16.9	31.1	23.5	20.6	14.7	10.0
≥75	9,992	8.4	20.8	19.6	21.8	20.1	17.7
Sex							
Men	54,968	46.4	26.1	24.8	17.7	16.5	14.8
Women	63,442	53.6	19.4	22.3	18.1	19.0	21.2
Number of conditions							
0	58,718	49.6	25.6	26.3	18.9	16.5	12.7
1	2,5755	21.8	22.2	22.9	17.8	18.1	18.9
2	14,677	12.4	21.1	21.5	17.3	18.6	21.6
≥3	19,260	16.3	14.6	17.2	15.6	20.8	31.7
Any psychiatric condition							
No	109,137	92.2	23.8	24.6	18.4	17.7	15.5
Yes	9,273	7.8	7.3	10.9	12.3	19.5	50.0
Total	118,410	100.0	22.5	23.5	18.0	17.8	18.2

PSS: Perceived Stress Scale

Table 2. Cumulative incidence proportions and incidence rate ratios of mental health related primary care activities according to Perceived Stress Scale quintile.

Primary care service	PSS quintile	CIP_{1y}(%)	95% CI	IR	Crude IRR	Adj. IRR*	95% CI
Talk therapy by GP	1	1.1	(1.0,1.2)	0.02	1	1	Reference
	2	1.7	(1.5,1.8)	0.03	1.48	1.38	(1.15,1.65)
	3	2.2	(2.0,2.4)	0.04	2.01	1.72	(1.43,2.06)
	4	3.1	(2.9,3.3)	0.06	2.76	2.38	(1.99,2.83)
	5	6.8	(6.5,7.2)	0.15	6.90	4.96	(4.20,5.86)
Psychometric tests	1	1.2	(1.1,1.3)	0.02	1	1	Reference
	2	1.8	(1.6,1.9)	0.02	1.38	1.26	(1.06,1.51)
	3	2.5	(2.3,2.7)	0.04	2.04	1.75	(1.46,2.10)
	4	3.2	(2.9,3.4)	0.05	2.82	2.16	(1.82,2.56)
	5	6.6	(6.2,6.9)	0.10	5.96	3.68	(3.11,4.35)
Psychologist services	1	0.4	(0.4,0.5)	0.02	1	1	Reference
	2	0.7	(0.6,0.8)	0.04	1.57	1.49	(1.08,2.05)
	3	1.2	(1.0,1.3)	0.06	2.54	1.99	(1.47,2.69)
	4	1.5	(1.4,1.7)	0.08	3.53	3.07	(2.26,4.16)
	5	3.3	(3.1,3.6)	0.21	8.69	6.49	(4.90,8.58)
Psychiatrist services	1	0.2	(0.1,0.3)	0.01	1	1	Reference
	2	0.3	(0.3,0.4)	0.02	2.17	1.96	(1.16,3.32)
	3	0.5	(0.4,0.6)	0.03	3.20	1.92	(1.07,3.46)
	4	0.9	(0.8,1.0)	0.06	6.86	4.61	(2.77,7.69)
	5	3.7	(3.4,4.0)	0.24	28.74	13.26	(8.33,21.09)
Antidepressants prescriptions	1	2.6	(2.4,2.8)	0.10	1	1	Reference
	2	3.7	(3.5,3.9)	0.16	1.55	1.28	(1.09,1.49)
	3	5.7	(5.4,6.0)	0.25	2.37	1.84	(1.58,2.16)
	4	8.6	(8.2,9.0)	0.40	3.85	2.35	(2.04,2.71)
	5	21.5	(20.9,22.0)	1.21	11.63	4.62	(4.03,5.31)
Anxiolytics prescriptions	1	1.5	(1.4,1.7)	0.03	1	1	Reference
	2	2.0	(1.8,2.2)	0.05	1.61	1.53	(1.29,1.83)
	3	2.8	(2.6,3.0)	0.08	2.59	2.02	(1.67,2.44)
	4	4.1	(3.8,4.4)	0.13	4.27	2.56	(2.16,3.03)
	5	9.4	(9.0,9.8)	0.46	14.52	4.73	(4.03,5.54)
Hypnotics prescriptions	1	3.4	(3.2,3.6)	0.08	1	1	Reference
	2	4.3	(4.0,4.5)	0.11	1.39	1.34	(1.18,1.51)
	3	5.3	(5.0,5.6)	0.16	2.03	1.67	(1.47,1.89)
	4	6.6	(6.3,7.0)	0.22	2.77	1.83	(1.61,2.07)
	5	11.0	(10.6,11.5)	0.5	6.32	2.93	(2.59,3.31)

PSS: Perceived Stress Scale. CI: Confidence interval. CIP_{1y}: Cumulative incidence proportion at one year (in %). IR: Incidence rate. IRR: Incidence rate ratio.

*: adjusted for sex, age as 10-year age bands, presence of each of the 39 psychiatric and physical conditions in the multimorbidity index, socioeconomic factors, and lifestyle on index date.

Table 3. Cumulative incidence proportions and incidence rate ratios of general primary care and chronic care services according to Perceived Stress Scale quintile.

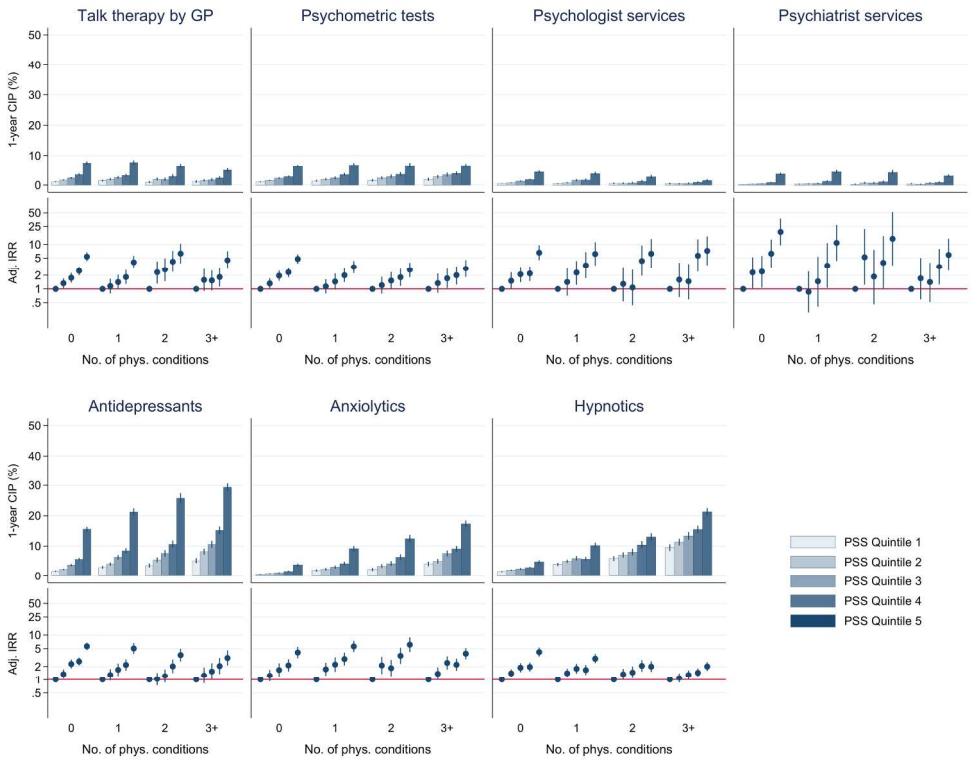
Primary care service	PSS quintile	CIP_{1y}(%)	95% CI	IR	Crude IRR	Adj. IRR*	95% CI
Spirometries	1	2.6	(2.4,2.8)	0.03	1	1	Reference
	2	3.0	(2.8,3.2)	0.04	1.15	1.12	(1.00,1.25)
	3	3.0	(2.8,3.3)	0.04	1.14	1.06	(0.94,1.19)
	4	3.6	(3.4,3.9)	0.05	1.40	1.17	(1.04,1.32)
	5	4.4	(4.1,4.6)	0.06	1.67	1.16	(1.03,1.31)
Blood sugar measures	1	13.9	(13.5,14.3)	0.21	1	1	Reference
	2	13.7	(13.3,14.1)	0.21	1.02	1.02	(0.97,1.07)
	3	14.7	(14.2,15.2)	0.23	1.08	1.05	(0.99,1.10)
	4	16.3	(15.8,16.8)	0.27	1.26	1.09	(1.04,1.15)
	5	18.4	(17.8,18.9)	0.3	1.44	1.12	(1.06,1.18)
ECGs	1	7.4	(7.1,7.7)	0.08	1	1	Reference
	2	7.7	(7.4,8.0)	0.09	1.03	1.05	(0.99,1.12)
	3	8.0	(7.6,8.4)	0.09	1.10	1.08	(1.02,1.16)
	4	9.2	(8.9,9.6)	0.11	1.29	1.17	(1.09,1.25)
	5	9.6	(9.3,10.1)	0.11	1.32	1.14	(1.07,1.22)
Home blood pressure measures	1	5.2	(4.9,5.5)	0.07	1	1	Reference
	2	5.2	(5.0,5.5)	0.07	0.99	1.05	(0.96,1.14)
	3	5.3	(5.0,5.6)	0.07	1.01	1.04	(0.95,1.14)
	4	5.6	(5.3,6.0)	0.08	1.11	1.10	(1.00,1.20)
	5	5.2	(4.9,5.5)	0.07	0.97	1.02	(0.93,1.13)
Annual chronic care consultations	1	18.1	(17.6,18.5)	0.31	1	1	Reference
	2	17.9	(17.5,18.4)	0.31	1.01	1.02	(0.97,1.06)
	3	18.7	(18.2,19.2)	0.33	1.09	1.04	(0.99,1.10)
	4	21.0	(20.4,21.5)	0.39	1.27	1.09	(1.04,1.14)
	5	23.8	(23.2,24.4)	0.47	1.53	1.22	(1.16,1.29)
Out-of-hours contacts	1	14.2	(13.8,14.7)	0.21	1	1	Reference
	2	16.1	(15.7,16.5)	0.25	1.16	1.07	(1.02,1.13)
	3	17.4	(16.9,18.0)	0.28	1.32	1.13	(1.07,1.19)
	4	19.7	(19.1,20.2)	0.33	1.57	1.22	(1.16,1.29)
	5	26.1	(25.6,26.7)	0.54	2.57	1.47	(1.39,1.55)
Daytime consultations	1	77.4	(76.9,77.9)	3.22	1	1	Reference
	2	79.9	(79.4,80.4)	3.46	1.07	1.04	(1.02,1.06)
	3	82.1	(81.6,82.6)	3.82	1.18	1.10	(1.07,1.12)
	4	84.7	(84.2,85.2)	4.45	1.38	1.18	(1.16,1.20)
	5	88.7	(88.3,89.2)	5.5	1.71	1.28	(1.25,1.30)

PSS: Perceived Stress Scale. CI: Confidence interval. CIP_{1y}: Cumulative incidence proportion at one year (in %). IR: Incidence rate. IRR: Incidence rate ratio.

*: adjusted for sex, age as 10-year age bands, presence of each of the 39 psychiatric and physical conditions in the multimorbidity index, socioeconomic factors, and lifestyle on index date.

Figure 1. Cumulative incidence proportions and incidence rate ratios of mental health related primary care services according to Perceived Stress Scale quintile and number of physical conditions.

Figure 2. Cumulative incidence proportions and incidence rate ratios of general primary care and chronic care services according to Perceived Stress Scale quintile and number of physical conditions.



Cumulative incidence proportions and incidence rate ratios of mental health related primary care services according to Perceived Stress Scale quintile and number of physical conditions.

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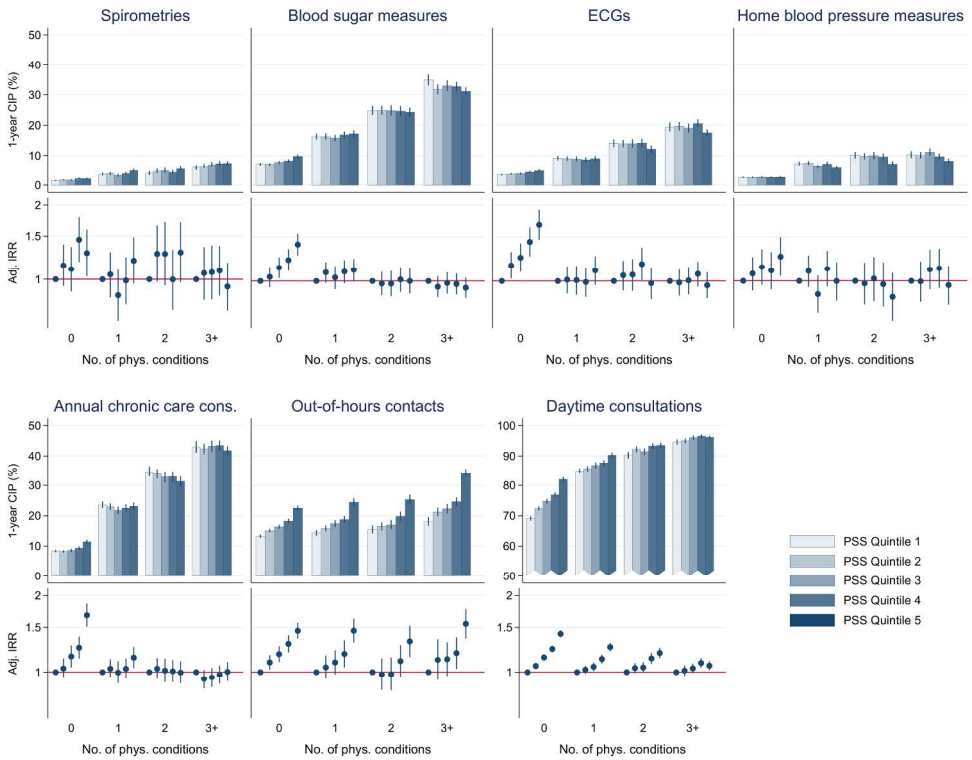

Cumulative incidence proportions and incidence rate ratios of general primary care and chronic care services according to Perceived Stress Scale quintile and number of physical conditions.

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Supplemental file

The association between perceived stress, multimorbidity, and primary care health services – a Danish population-based cohort study

eTable 1. Multimorbidity index diseases

Category	Disease group
Circulatory system	Hypertension
	Dyslipidemia
	Ischemic heart disease
	Atrial fibrillation
	Heart failure
	Peripheral artery occlusive disease
	Stroke
Endocrine system	Diabetes mellitus
	Thyroid disorder
	Gout
Pulmonary system and allergy	Chronic pulmonary disease
	Allergy
Gastrointestinal system	Ulcer/chronic gastritis
	Chronic liver disease
	Inflammatory bowel disease
	Diverticular disease of intestine
Urogenital system	Chronic kidney disease
	Prostate disorders
Musculoskeletal system	Connective tissue disorders
	Osteoporosis
	Painful condition
Haematological system	Anaemias
	HIV/AIDS
Cancers	Cancer
Neurological system	Vision problem
	Hearing problem
	Migraine
	Epilepsy
	Parkinson's disease
	Multiple sclerosis
	Neuropathies
Mental health conditions	Mood, stress-related, or anxiety disorders
	Psychological distress
	Alcohol problems
	Substance abuse
	Anorexia/bulimia
	Bipolar affective disorder
	Schizophrenia or schizoaffective disorder
	Dementia

HIV: human immunodeficiency virus; AIDS: acquired immunodeficiency syndrome.

[a]For details and coding definitions, please see Prior A, Fenger-Grøn M, Larsen KK, et al. The association between perceived stress and mortality among people with multimorbidity: A prospective population-based cohort study. Am J Epidemiol 2016;184:199-210.

eTable 2. Classification codes for services and prescriptions

Outcome	Danish National Health Service Register service codes*	ATC prescription codes
Talk therapy by GP	4003, 4021-4027, 4050, 4063, 4106, 4247-4249, 6101 (daytime)	
Psychometric tests	2149 (daytime)	
Psychologist services	0100-0299, 1000-3999 (daytime)	
Psychiatrist services	0110-0140, 0210-0236 (daytime)	
Antidepressant prescriptions		N06AB, N06AF, N06AG, N06AX (N06AX12 & N06AX05 excluded)
Anxiolytics prescriptions		N05BA, N05BE
Hypnotics prescriptions		N05CD, N05CF, N05CH
Daytime consultations	0101 (daytime)	
Out-of-hours contacts (telephone, consultations, home visits)	0501, 0602, 04XX (out-of-hours)	
Annual chronic care consultations	0106, 0120 (daytime)	
Spirometries	7113 (daytime)	
Blood sugar measures	7136 (daytime)	
ECGs	7156 (daytime)	
Home blood pressure measures	2146 (daytime)	

ATC: Anatomical Therapeutic Chemical classification.
* Provider specialty is general practice (codes 80-89), except for psychologists services (code 63) and psychiatrist services (code 24).

eTable 3. Incidence rate ratios of primary care services according to Perceived Stress Scale quintile for persons without psychiatric illness (N=109,137)

Activity	PSS quintile	Adj. IRR*	95% CI	Activity	PSS quintile	Adj. IRR*	95% CI
Talk therapy by GP	1	1	Reference	Spirometries	1	1	Reference
	2	1.36	(1.12,1.66)		2	1.10	(0.98,1.24)
	3	1.61	(1.32,1.96)		3	1.07	(0.94,1.21)
	4	2.39	(1.98,2.89)		4	1.15	(1.01,1.30)
	5	5.22	(4.36,6.26)		5	1.16	(1.01,1.32)
Psychometric tests	1	1	Reference	Blood sugar measures	1	1	Reference
	2	1.26	(1.05,1.52)		2	1.03	(0.98,1.08)
	3	1.78	(1.47,2.16)		3	1.06	(1.00,1.11)
	4	2.14	(1.78,2.58)		4	1.09	(1.04,1.16)
	5	3.99	(3.33,4.78)		5	1.12	(1.06,1.19)
Psychologist services	1	1	Reference	ECGs	1	1	Reference
	2	1.53	(1.09,2.15)		2	1.05	(0.99,1.12)
	3	1.97	(1.43,2.72)		3	1.08	(1.01,1.16)
	4	3.05	(2.21,4.23)		4	1.16	(1.09,1.24)
	5	6.83	(5.05,9.23)		5	1.15	(1.07,1.24)
Psychiatrist services	1	1	Reference	Home blood pressure measures	1	1	Reference
	2	2.17	(1.12,4.19)		2	1.06	(0.97,1.15)
	3	2.32	(1.14,4.71)		3	1.04	(0.95,1.14)
	4	5.69	(3.08,10.52)		4	1.09	(1.00,1.20)
	5	25.45	(14.54,44.54)		5	1.04	(0.93,1.15)
Antidepressants prescriptions	1	1	Reference	Annual chronic care consultation	1	1	Reference
	2	1.30	(1.04,1.63)		2	1.03	(0.98,1.07)
	3	2.22	(1.78,2.76)		3	1.05	(1.00,1.11)
	4	2.84	(2.31,3.50)		4	1.09	(1.04,1.15)
	5	6.79	(5.59,8.25)		5	1.24	(1.17,1.31)
Anxiolytics prescriptions	1	1	Reference	Out-of-hours contacts	1	1	Reference
	2	1.54	(1.27,1.87)		2	1.07	(1.01,1.13)
	3	2.07	(1.69,2.55)		3	1.13	(1.07,1.19)
	4	2.67	(2.21,3.24)		4	1.23	(1.16,1.30)
	5	5.01	(4.18,6.00)		5	1.47	(1.39,1.55)
Hypnotics prescriptions	1	1	Reference	Daytime consultations	1	1	Reference
	2	1.33	(1.17,1.51)		2	1.04	(1.02,1.06)
	3	1.61	(1.41,1.84)		3	1.09	(1.07,1.12)
	4	1.86	(1.63,2.12)		4	1.17	(1.14,1.19)
	5	2.96	(2.59,3.38)		5	1.28	(1.25,1.31)

PSS: Perceived Stress Scale. IRR: Incidence rate ratio.

*: adjusted for sex, age as 10-year age bands, presence of each of the 39 psychiatric and physical conditions in the multimorbidity index, socioeconomic factors, and lifestyle on index date.

eTable 4. Incidence rate ratios for primary care activities requested by non-respondents versus respondents

Activity	Non-respondent crude IRR	95% CI	Non-respondent adjusted IRR*	95% CI
Talk therapy by GP	1.18	(1.11,1.25)	1.23	(1.15,1.31)
Psychometric tests	1.20	(1.13,1.27)	1.14	(1.07,1.22)
Psychologist services	0.93	(0.85,1.02)	0.95	(0.83,1.09)
Psychiatrist services	1.32	(1.20,1.46)	1.46	(1.23,1.73)
Antidepressant prescriptions	1.96	(1.88,2.03)	1.46	(1.37,1.56)
Anxiolytics prescriptions	2.34	(2.20,2.48)	1.93	(1.78,2.09)
Hypnotics prescriptions	1.70	(1.62,1.79)	1.38	(1.30,1.47)
Spirometries	0.86	(0.81,0.91)	0.94	(0.88,0.99)
Blood sugar measures	0.94	(0.91,0.96)	0.97	(0.95,1.00)
ECGs	0.82	(0.79,0.85)	0.88	(0.86,0.91)
Home blood pressure measures	0.74	(0.70,0.77)	0.88	(0.84,0.93)
Annual chronic care consultation	0.88	(0.86,0.90)	0.93	(0.91,0.96)
Out-of-hours contacts	1.59	(1.51,1.68)	1.20	(1.17,1.23)
Daytime consultations	0.94	(0.93,0.95)	0.95	(0.94,0.96)

IRR: Incidence rate ratios.
*: IRRs adjusted for sex, age as 10-year age bands, presence of each of the 39 psychiatric and physical conditions in the multimorbidity index, cohabitation status, and educational level on index date.
The reference for each activity is survey respondents.

eTable 5. Incidence rate ratios for general primary care services in persons with any psychiatric condition versus persons without psychiatric conditions according to survey response status

		Respondents		Non-respondents	
Activity	Any psychiatric condition	Adj. IRR	95% CI	Adj. IRR	95% CI
Annual chronic care consultation	No	1	Reference	1	Reference
	Yes	1.39	(1.15,1.68)	1.26	(1.04,1.53)
Out-of-hours contacts	No	1	Reference	1	Reference
	Yes	1.77	(1.43,2.18)	1.85	(1.50,2.28)
Daytime consultations	No	1	Reference	1	Reference
	Yes	1.35	(1.24,1.48)	1.33	(1.21,1.45)

IRR: Incidence rate ratios.

*: IRRs adjusted for sex, age as 10-year age bands, presence of each of the 39 psychiatric and physical conditions in the multimorbidity index, cohabitation status and educational level on index date.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Described on page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1–2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2–3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5–7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5–6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5–7, eTable 1 eTable 2
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6–7, eTable 1 eTable 2
Bias	9	Describe any efforts to address potential sources of bias	7–8
Study size	10	Explain how the study size was arrived at	5–6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6–8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	8
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods	6–8

		taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5, 8
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8, 9, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	9
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	8 Table 2–3
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8, 9, Table 2–3
		(*b*) Report category boundaries when continuous variables were categorized	Table 1
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Table 2–3
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10, Figure 1–2 eTable 3, eTable 4, eTable 5
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11–12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12–14
Generalisability	21	Discuss the generalisability (external validity) of the study results	11, 13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at

http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.