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Diagnoses Documented Before the First Recorded Burnout Diagnosis in German General Practices: A Matched Case–Control Study

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Abstract

Background: Burnout is frequently documented in German general practice, but little is known about which complaints are recorded beforehand. Methods: This matched case–control study used the Disease Analyzer database (IQVIA) and included adults aged 18–65 years with a first documented burnout diagnosis (International Classification of Diseases, 10th revision: Z73.0) in German general practices between 2005 and 2025 and at least 12 months of prior observation. Each case was matched exactly to five controls without any burnout diagnosis on age, sex, health insurance, and index year. Thirty-eight diagnosis groups were assessed in two windows (0–6 and 6–12 months prior to the index date, specifically corresponding to days 1–183 and 184–365, respectively) using multivariable logistic regression with practice-level clustering and false discovery rate correction. Results: We analysed 24,932 cases and 124,660 controls (mean age 44.9 years, 42.7% male). In the 6 months directly before the index date, associations were strongest for problems related to employment (odds ratio 2.94; 95% confidence interval [CI] 2.33–3.72), neurasthenia (2.85; 2.48–3.28), malaise and fatigue (2.39; 2.16–2.65), and reaction to severe stress (2.02; 1.80–2.26). All were weaker in the earlier window; back pain and respiratory infections showed no such gradient. At least one symptom diagnosis was documented in 45.9% of cases versus 26.2% of controls, and an exhaustion- or stress-related diagnosis in 26.5% versus 9.6%. Absolute case–control differences were nearly identical in female and male patients. Conclusions: Diagnoses documented before a first recorded burnout diagnosis were concentrated in the final six months and were dominated by exhaustion- and stress-related codes. These findings describe patterns of clinical documentation rather than validated early indicators of burnout. In most patients, however, nothing of this kind is recorded, which limits what routine data can contribute to early identification.

Keywords: burnout; professional; primary health care; general practice; electronic health records; occupational stress; case-control studies

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1. Introduction

Burnout is conceptualised as a syndrome arising from chronic workplace stress that has not been successfully managed, characterised by exhaustion, mental distance from work, and reduced professional efficacy (Maslach & Leiter, 2016). The term was introduced in the

1970s to describe the progressive emotional depletion observed in human service workers, and the concept has since been extended from an occupational–psychological description to a condition with recognised psychobiological correlates (Nadon et al., 2022). Despite five decades of research, it has not been established as a disease entity. In the 11th revision of the International Classification of Diseases (World Health Organization, 2022), it is listed as an occupational phenomenon rather than a medical condition, in the chapter covering reasons for contact with health services that are not classified as illnesses; in the 10th revision, which still governs outpatient coding in Germany, the corresponding entry is Z73.0 in the same category (Edú-Valsania et al., 2022). Measurement has remained equally heterogeneous, with numerous instruments, cut-offs, and case definitions in use (Edú-Valsania et al., 2022), which is one reason why epidemiological estimates vary widely between studies.

The conceptual overlap with depression has been debated for many years. A systematic review and meta-analysis found a substantial but incomplete correlation between burnout and depressive symptoms and concluded that the two constructs remain distinguishable (Koutsimani et al., 2019). In Sweden, the related diagnosis of exhaustion disorder was introduced precisely to give the clinical picture a formal place in the classification, and research on it has expanded rapidly since (Lindsäter et al., 2022). Clinically, this picture extends well beyond low mood: reviews of clinical burnout describe sleep impairment, cognitive disturbance, and a range of neurobiological and physiological alterations as core rather than incidental features (Grossi et al., 2015).

The health consequences of sustained occupational strain are well documented. A systematic review of prospective studies reported associations of burnout with subsequent physical, psychological, and occupational outcomes, including cardiovascular disease, musculoskeletal pain, insomnia, and prolonged sickness absence (Salvagioni et al., 2017). Chronic stress affects health through neuroendocrine, autonomic, and inflammatory pathways and is an established risk and prognostic factor for cardiovascular disease (Kivimäki & Steptoe, 2018; O'Connor et al., 2021). Burnout itself has been linked to sustained autonomic activation, altered cortisol regulation, low-grade inflammation, and structural and functional brain changes (Bayes et al., 2021). Several of the symptom complexes that patients present with in general practice are themselves stress-sensitive: irritable bowel syndrome and other functional gastrointestinal disorders are strongly linked to psychological distress and are among the most common conditions worldwide (Ford et al., 2020; Sperber et al., 2021), migraine affects around one in ten people and is frequently triggered and aggravated by stress (Ashina et al., 2021), and tinnitus is highly prevalent and closely associated with psychological burden (Jarach et al., 2022). Somatoform disorders and medically unexplained symptoms are more common in primary care than generally assumed (Haller et al., 2015).

There are good reasons to expect that burnout is preceded by a phase in which such complaints become apparent. Burnout is conceptualised as the endpoint of a gradual process rather than as an acute event, and prospective work supports this: in a Swedish cohort of working individuals, insufficient sleep at baseline was the main predictor of clinical burnout over the following two years, alongside high work demands (Söderström et al., 2012). Patients who present to specialised clinics with stress-related exhaustion report a heavy burden of somatic complaints, most commonly gastrointestinal symptoms, headache, and dizziness (Glise et al., 2014). If these complaints bring patients to their general practitioner before the burnout entry is made, they should be traceable in routine documentation.

In Germany, general practitioners are the professional group that both identifies and records burnout, and the code is used on a considerable scale: in a previous analysis of German general practices, burnout was documented in 3.6% to 3.8% of working-age patients

in three consecutive three-year periods between 2012 and 2022, with stable prevalence but increasing duration of related sick leave (Kostev et al., 2024). Burnout is also prevalent among general practitioners themselves, which shapes awareness of the condition in this setting (Dreher et al., 2019). Evidence on what is documented before the entry, however, is scarce. A retrospective chart review at a single Swedish primary healthcare centre examined the presenting complaints of 115 patients in the two years before they received a diagnosis of exhaustion disorder and found stress-related complaints to be common (Adamsson & Bernhardsson, 2018), but the study had no comparison group and could therefore not establish whether these complaints were more frequent than in patients who did not go on to receive the diagnosis.

Using nationwide data from German general practices, we therefore examined which diagnoses were documented in the 12 months preceding a burnout index diagnosis compared with matched individuals without such a diagnosis, whether these diagnoses concentrated in the six months closest to the index, what proportion of patients showed any documented complaint at all, and whether the pattern differed between female and male patients. The overarching aim was to clarify what routine primary care documentation can realistically contribute to the earlier recognition of occupational strain, and thereby to inform clinical practice and policies on the documentation of stress-related complaints.

2. Materials and Methods

2.1. Study Design, Setting, and Data Source

This retrospective matched case–control study was conducted in German primary care using data from the Disease Analyzer database (IQVIA). This data source has already been used in several previous studies focusing on psychiatric disorders (Kostev et al., 2026), including work on burnout in German general practices (Kostev et al., 2024), and contains anonymous data on diagnoses, prescriptions, and basic demographic data from computer systems used in office-based practices (Rathmann et al., 2018). The database contains approximately 3000 office-based practices, including general practitioners and specialists in Germany. The sampling method for the Disease Analyzer database uses statistics from the German Medical Association to determine the panel design according to specialist group, German federal state, community size category, and age of physician. It has previously been shown that the panel of practices included in the Disease Analyzer database is representative of general and specialised practices in Germany (Rathmann et al., 2018). The present analysis was restricted to general practices; practices with a diabetology focus were excluded. Data are transferred directly from the practice computer systems in anonymous form; diagnoses are coded according to the German modification of the International Classification of Diseases, 10th revision (ICD-10-GM), and prescriptions according to the Anatomical Therapeutic Chemical classification of the European Pharmaceutical Market Research Association (EphMRA). Cases and controls were identified by electronic queries of the database.

2.2. Study Population

Cases were individuals aged 18 to 65 years with a first documented diagnosis of burnout (ICD-10: Z73.0) in 1183 general practices in Germany between January 2005 and December 2025. The date of this first documentation defined the index date. A further inclusion criterion was an observation time of at least 12 months prior to the index date, ensuring patient observability during the two analysis periods: 0–6 months directly preceding the index date and 6–12 months before the index date.

Controls were individuals without any documented burnout diagnosis over their entire available history in the database. For these individuals, the index date was a randomly selected visit date between January 2005 and December 2025. The same age, calendar period, and observation time criteria were applied as for the cases. Accordingly, patients were excluded if they were younger than 18 or older than 65 years at the index date, if the index date fell outside the period from January 2005 to December 2025, or if they had been observed in the practice for less than 12 months before the index date; individuals with a burnout diagnosis at any time were excluded from the pool of potential controls.

Controls were matched to cases in a 1:5 ratio using exact matching on age in single years, sex, type of health insurance (statutory or private), and index year. A propensity score derived from these four variables was used only to determine the order of selection within the exact-match strata; the matching itself was exact, and each control was used only once. Every case was assigned exactly five controls. The flow diagram of study patients is shown in Figure 1.

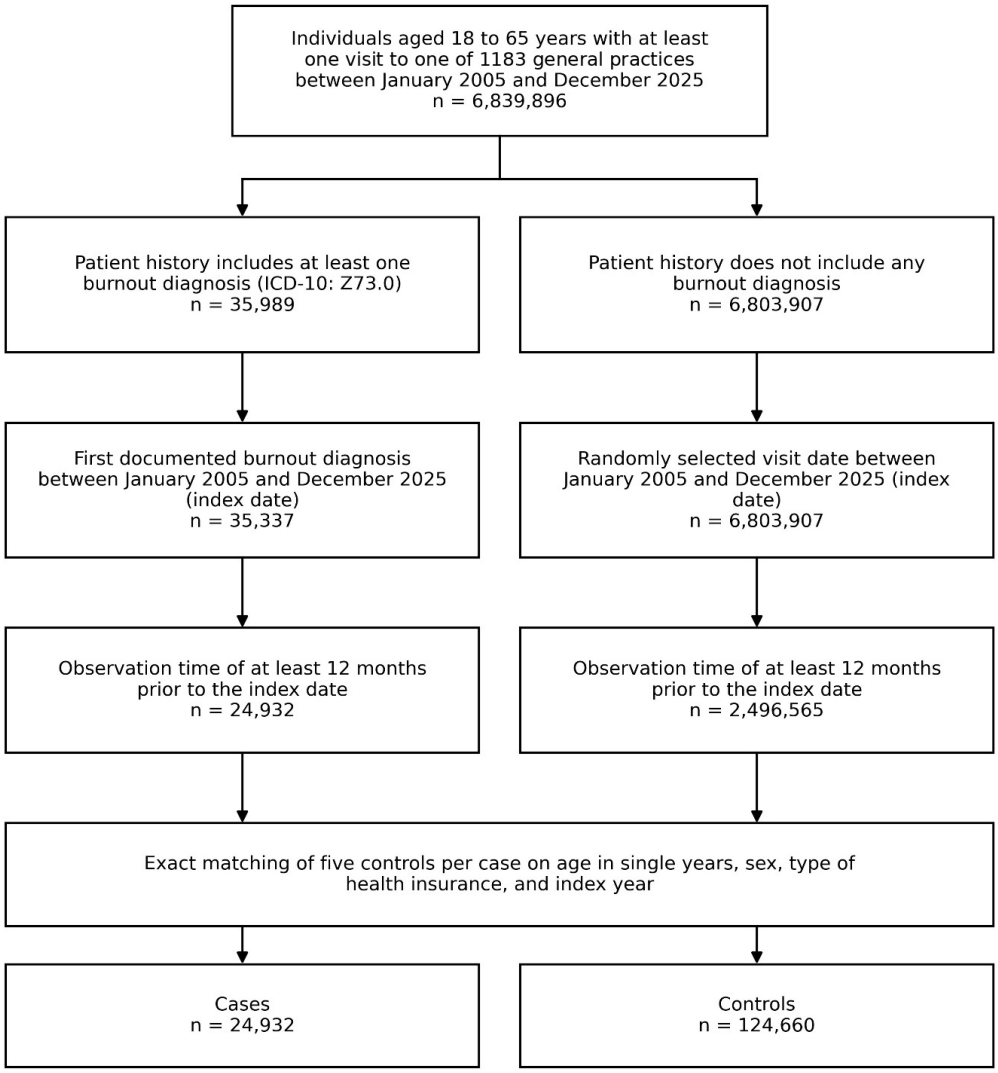


Figure 1. Selection of cases and controls. ICD-10, International Classification of Diseases, 10th revision.

2.3. Study Variables

All diagnoses documented in the general practice prior to the index date were assigned to two mutually exclusive time windows: the 6 months immediately preceding the index date, excluding the index date itself, and months 6 to 12 prior to the index date. A diagnosis group was considered present in a given analysis window if at least one corresponding entry was documented within that window.

The selection of these diagnosis groups was based on the clinical literature on burnout and stress-related exhaustion rather than on a data-driven procedure. It comprised the symptom complexes repeatedly described in patients with clinical burnout or exhaustion disorder, in particular exhaustion, sleep impairment, and cognitive disturbance (Grossi et al., 2015; Lindsäter et al., 2022; Söderström et al., 2012); the somatic complaints most frequently reported by patients presenting with stress-related exhaustion, namely gastrointestinal symptoms, headache, and dizziness (Glise et al., 2014); and the presenting complaints recorded before a diagnosis of exhaustion disorder in primary care (Adamsson & Bernhardsson, 2018). Diagnoses were grouped at the level of three- or four-digit ICD-10 codes so that the definitions remain reproducible in routine data.

Thirty-eight diagnosis groups were defined a priori as diagnoses of interest (Table 1).

Table 1. Diagnosis groups of interest and corresponding ICD-10 codes.

Category	Diagnosis Group	ICD-10 Code(s)
Ear-related diagnoses	Sudden idiopathic hearing loss	H91.2
	Tinnitus	H93.1
Functional gastrointestinal diagnoses	Gastro-oesophageal reflux disease	K21
	Gastritis	K29
	Functional dyspepsia	K30
	Irritable bowel syndrome	K58
	Constipation or other functional intestinal disorders	K59
Infectious and dermatological diagnoses	Herpes labialis and herpes zoster	B00, B02
	Acute respiratory tract infections	J00–J06, J20
	Selected chronic skin diagnoses	L20, L40, L50, L63
	Urinary tract infections	N30, N39.0
Mental and behavioural diagnoses	Sedative or hypnotic use disorder	F13
	Depressive episode and recurrent depressive disorder	F32, F33
	Other anxiety disorders	F41
	Reaction to severe stress and adjustment disorders	F43
	Somatoform disorders	F45
	Neurasthenia	F48.0
	Sleep disorders	G47, F51
Other diagnoses	Thyroid disorders	E00–E07
	Problems related to employment	Z56
Pain and musculoskeletal diagnoses	Migraine	G43
	Tension-type headache	G44.2
	Joint pain	M25.5
	Neck and shoulder complaints	M53, M75
	Back pain	M54
	Myalgia and fibromyalgia	M79

Table 1. *Cont.*

Category	Diagnosis Group	ICD-10 Code(s)
Symptom diagnoses	Palpitations	R00.2
	Dyspnoea	R06
	Chest pain	R07
	Abdominal pain or nausea	R10, R11
	Disturbances of skin sensation	R20
	Disturbances of cognition and orientation	R41
	Dizziness	R42
	Nervousness and irritability	R45
	Unspecific headache	R51
	Malaise and fatigue	R53
	Hyperhidrosis	R61
	Changes in appetite or weight	R63

A further set of diagnoses was included in all models as covariates but is not reported as a study result, because these conditions were considered potential confounders rather than diagnoses of interest (Table 2). This distinction does not imply that these conditions are unrelated to stress: psychosocial stress is associated with hypertension (Liu et al., 2017), depression with incident type 2 diabetes (Graham et al., 2020), and chronic stress is an established risk factor for cardiovascular disease (Kivimäki & Steptoe, 2018). The criterion was whether the documentation of a diagnosis within the 12 months before the index date could plausibly reflect a complaint presented in that period. The diagnoses of interest are largely symptom-based, are made on the basis of what the patient reports, and can appear and resolve within weeks or months. The covariate diagnoses, in contrast, are chronic conditions that develop over years, are established by objective criteria such as blood pressure, laboratory values, or imaging, and are documented repeatedly once diagnosed; their documentation in a given window therefore mainly reflects long-standing morbidity, which influences consultation frequency and documentation. For transparency, their estimates are shown in Supplementary Table S6.

The two substance use disorders were also handled as covariates rather than diagnoses of interest due to their infrequent and inconsistent documentation in German primary care and were therefore not considered informative as separate results. A further covariate was the number of practice contacts within each time window: these were added up during each analysis period and truncated at 24 contacts in order to limit the influence of extreme values.

In addition to the individual diagnosis groups, three composite variables were derived. A broad definition comprised all diagnoses interpretable as a symptom presentation prior to the burnout entry and excluded the covariate diagnoses, thyroid disorders, acute respiratory tract infections, urinary tract infections, chronic skin diagnoses, and problems related to employment. A narrow definition, referred to below as the exhaustion and stress complex, comprised neurasthenia, malaise and fatigue, reaction to severe stress and adjustment disorders, sleep disorders, depression, somatoform disorders, and anxiety disorders. A conservative variant corresponded to the broad definition without depression and without back pain. For each definition, a patient was classified as positive within a given analysis window if at least one of the included diagnoses was documented in that window. The number of distinct diagnosis groups documented per window was counted as a measure of symptom burden. The three definitions were specified in order to examine whether the findings depended on how broadly a symptom presentation was defined: the broad definition captures any complaint plausibly presented as a symptom, the exhaustion and stress complex restricts this to the diagnoses that correspond most directly to the burnout

construct (Grossi et al., 2015; Maslach & Leiter, 2016), and the conservative definition additionally excludes depression and back pain, the two groups most likely to represent an independent condition rather than a complaint preceding the burnout entry.

Table 2. Diagnoses included as covariates.

Covariate Category	Diagnosis	ICD-10 Code(s)
Cardiometabolic and cardiovascular	Diabetes mellitus	E10–E14
	Obesity	E65–E68
	Dyslipidaemia	E78
	Valvular heart disease	I05–I09, I34–I39
	Hypertension	I10
	Coronary heart disease	I24, I25
	Atrial fibrillation	I48
	Heart failure	I50
	Angina pectoris	I20
Malignancy	Cancer	C00–C97
Musculoskeletal	Osteoporosis	M80, M81
Neurological	Parkinson's disease	G20, G21
	Epilepsy	G40, G41
	Transient ischaemic attack	G45
Renal	Chronic kidney disease	N18, N19
Respiratory	Chronic obstructive pulmonary disease	J44
Substance use disorders	Alcohol use disorder	F10
	Tobacco use disorder	F17

For a supplementary analysis, prescriptions issued in the two time windows were extracted for six drug classes chosen as indicators of the perceived severity of the documented complaints: antidepressants (N06A), hypnotics and sedatives (N05B), tranquillisers (N05C), non-steroidal anti-inflammatory drugs (M01A), analgesics (N02A, N02B), and antiulcerants (A02B). A patient was classified as exposed if at least one prescription of the respective class was documented in the window.

2.4. Statistical Analyses

Proportions of patients with each diagnosis group and with each composite definition were compared between cases and controls for both time windows. The association between each diagnosis group and burnout documentation was assessed using multivariable logistic regression with burnout status as the dependent variable. Separate models were fitted for each time window. All diagnoses of interest and all covariate diagnoses of the respective window entered the model simultaneously alongside the patients' sex, type of health insurance, age group (18–30 years [reference], 31–45, 46–55, and 56–65 years), index year group (2005–2008 [reference], 2009–2012, 2013–2016, 2017–2019, 2020–2022, and 2023–2025), and the number of practice contacts within the window. Because patients were clustered within practices, all models were estimated with Taylor series linearised variance estimation using the practice as the cluster variable. Results are displayed as odds ratios (ORs) with 95% confidence intervals (CIs). A sensitivity analysis repeated all models without adjustment for the number of practice contacts.

Unconditional logistic regression adjusted for the matching variables was chosen as the main approach because matching was performed on a small number of broad demographic variables, so that each case could have been matched to many other eligible controls. Under

such loose matching, an unconditional analysis that controls for the matching factors yields valid estimates without loss of precision (Kuo et al., 2018; Pearce, 2016) and, unlike conditional logistic regression, allows the clustering of patients within practices to be taken into account. To assess whether the results depended on this choice, all models were re-estimated using conditional logistic regression stratified by matched set, adjusted for the number of practice contacts and all diagnoses of the respective window.

Because the study period included the COVID-19 pandemic, and fatigue and cognitive impairment are among the most frequent features of post-COVID-19 condition (Ceban et al., 2022), all models were repeated separately for index dates in 2005–2019, 2020–2022, and 2023–2025, with the index year as an additional adjustment variable. In a further analysis, all models were repeated after excluding all patients with a documented COVID-19 diagnosis or post-COVID-19 condition (ICD-10-GM U07.1, U07.2, U08, U09) at any time before the index date. Prescriptions of the six drug classes were compared between cases and controls and analysed in the same way as the composite definitions. Finally, to describe the extent to which the documented diagnoses discriminate between cases and controls, the area under the receiver operating characteristic curve (c-statistic) was estimated for three nested models (matching variables and practice contacts; additionally the covariate diagnoses; additionally all diagnoses of interest), and the sensitivity and specificity of each composite definition were calculated. The results of these additional analyses are presented in Supplementary Tables S2–S5.

To account for multiple testing, *p*-values for the diagnoses of interest were adjusted using the Benjamini–Hochberg procedure to control the false discovery rate (FDR) across all 76 tests, corresponding to 38 diagnosis groups analysed within two time windows. Covariate diagnoses were not included in this correction. A two-sided FDR-adjusted *p*-value of less than 0.05 was considered statistically significant.

Differences between female and male patients were examined in two ways. First, all models were repeated separately for female and male patients. Second, interaction terms between sex and each diagnosis of interest were added to the pooled model, and the corresponding *p*-values were used as a formal test of effect modification, again with correction across all interaction tests. Because the documentation of symptom diagnoses differs between female and male patients at baseline, differences between the sexes were interpreted on the absolute scale, that is, as the difference in proportions between cases and controls within each sex, in addition to the multiplicative scale. Analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA).

3. Results

3.1. Basic Characteristics of the Study Sample

Of 6,839,896 individuals aged 18 to 65 years with at least one visit to one of 1183 general practices between January 2005 and December 2025, 35,989 had at least one documented burnout diagnosis. After applying the calendar period and observation time criteria, 24,932 cases and 124,660 matched controls were included (Figure 1). Because matching was exact, the two groups were identical with respect to all matching variables. Mean age was 44.9 years (standard deviation 11.9) in both groups, with 14.4% of patients aged 18 to 30 years, 34.4% aged 31 to 45 years, 27.8% aged 46 to 55 years, and 23.4% aged 56 to 65 years. Male patients accounted for 42.7% of the study sample and 8.1% were privately insured. Index dates were distributed unevenly across the study period, with 3.3% falling between 2005 and 2008 and 34.7% between 2023 and 2025 (Table 3).

Table 3. Characteristics of cases and controls.

Characteristic	Cases (n = 24,932)	Controls (n = 124,660)
Age, mean (standard deviation), years	44.9 (11.9)	44.9 (11.9)
18 to 30 years, n (%)	3582 (14.4)	17,910 (14.4)
31 to 45 years, n (%)	8587 (34.4)	42,935 (34.4)
46 to 55 years, n (%)	6918 (27.8)	34,590 (27.8)
56 to 65 years, n (%)	5845 (23.4)	29,225 (23.4)
Female patients, n (%)	14,282 (57.3)	71,410 (57.3)
Male patients, n (%)	10,650 (42.7)	53,250 (42.7)
Statutory health insurance, n (%)	22,906 (91.9)	114,530 (91.9)
Private health insurance, n (%)	2026 (8.1)	10,130 (8.1)
Index date 2005 to 2008, n (%)	812 (3.3)	4060 (3.3)
Index date 2009 to 2012, n (%)	2939 (11.8)	14,695 (11.8)
Index date 2013 to 2016, n (%)	2949 (11.8)	14,745 (11.8)
Index date 2017 to 2019, n (%)	4104 (16.5)	20,520 (16.5)
Index date 2020 to 2022, n (%)	5487 (22.0)	27,435 (22.0)
Index date 2023 to 2025, n (%)	8641 (34.7)	43,205 (34.7)

Cases and controls were matched exactly on age in single years, sex, type of health insurance, and index year; the distributions of these variables are therefore identical by design.

3.2. Diagnoses Documented Before the Index Date

During the 6 months immediately preceding the index date, 20 of the 38 diagnosis groups were significantly associated with a subsequent burnout entry after correction for multiple testing, and 19 in the window covering months 6 to 12. No diagnosis group was associated with lower odds of burnout documentation after correction.

The strongest associations were observed for problems related to employment (OR 2.94; 95% CI 2.33–3.72), neurasthenia (OR 2.85; 95% CI 2.48–3.28), malaise and fatigue (OR 2.39; 95% CI 2.16–2.65), and reaction to severe stress and adjustment disorders (OR 2.02; 95% CI 1.80–2.26), all in the 6 months preceding the index date. Further associations of moderate magnitude were found for tinnitus (OR 1.77), sudden hearing loss (OR 1.75), sleep disorders (OR 1.67), depression (OR 1.64), migraine (OR 1.54), somatoform disorders (OR 1.52), acute respiratory tract infections (OR 1.51), palpitations (OR 1.50), nervousness and irritability (OR 1.46), and dizziness (OR 1.45). Thyroid disorders, gastritis, gastro-oesophageal reflux disease, joint pain, urinary tract infections, and constipation were not associated with burnout documentation in either window (Table 4).

Associations were consistently weaker for diagnoses documented during the more distant time window (months 6–12 prior to the initial burnout entry). For the diagnoses most closely related to exhaustion and stress, the point estimates were lower for problems related to employment (OR 2.43 vs. 2.94), neurasthenia (OR 2.23 vs. 2.85), malaise and fatigue (OR 1.91 vs. 2.39), reaction to severe stress (OR 1.71 vs. 2.02), and depression (OR 1.34 vs. 1.64) compared to the 6 months directly preceding the index date. The corresponding proportions among cases showed the same pattern, for example, 2.2% versus 3.6% for neurasthenia, 3.9% versus 6.4% for malaise and fatigue, and 4.5% versus 7.0% for reaction to severe stress. Pain and infection diagnoses did not follow this gradient: back pain was documented in 13.0% of cases during the closer window and in 12.0% in the more distant window, with ORs of 1.14 and 1.28, and acute respiratory tract infections in 22.5% and 21.6%, with ORs of 1.51 and 1.63.

Table 4. Diagnoses documented before the index date in cases and controls.

Diagnosis Group	ICD-10 Code(s)	Months 0–6 Before the Index Date				Months 6–12 Before the Index Date			
		Cases n (%)	Controls n (%)	OR (95% CI)	*p*-Value	Cases n (%)	Controls n (%)	OR (95% CI)	*p*-Value
Thyroid disorders	E00–E07	1626 (6.5)	6131 (4.9)	1.02 (0.93–1.12)	0.727	1418 (5.7)	5467 (4.4)	0.99 (0.90–1.09)	0.859
Sleep disorders	G47, F51	1363 (5.5)	2095 (1.7)	1.67 (1.50–1.86)	<0.001	904 (3.6)	1650 (1.3)	1.53 (1.38–1.71)	<0.001
Depression	F32, F33	2327 (9.3)	4417 (3.5)	1.64 (1.48–1.81)	<0.001	1573 (6.3)	3613 (2.9)	1.34 (1.21–1.48)	<0.001
Back pain	M54	3235 (13.0)	10,545 (8.5)	1.14 (1.06–1.22)	<0.001	2984 (12.0)	8776 (7.0)	1.28 (1.19–1.37)	<0.001
Reaction to severe stress, adjustment disorders	F43	1756 (7.0)	2670 (2.1)	2.02 (1.80–2.26)	<0.001	1119 (4.5)	2035 (1.6)	1.71 (1.52–1.92)	<0.001
Other anxiety disorders	F41	717 (2.9)	1471 (1.2)	1.21 (1.05–1.38)	0.017	492 (2.0)	1153 (0.9)	1.16 (1.00–1.35)	0.096
Somatoform disorders	F45	1272 (5.1)	2229 (1.8)	1.52 (1.31–1.76)	<0.001	870 (3.5)	1842 (1.5)	1.28 (1.10–1.49)	0.004
Neurasthenia	F48.0	909 (3.6)	925 (0.7)	2.85 (2.48–3.28)	<0.001	555 (2.2)	744 (0.6)	2.23 (1.91–2.60)	<0.001
Sedative or hypnotic use disorder	F13	6 (0.0)	45 (0.0)	0.36 (0.14–0.90)	0.056	4 (0.0)	32 (0.0)	0.43 (0.14–1.31)	0.201
Malaise and fatigue	R53	1601 (6.4)	2179 (1.7)	2.39 (2.16–2.65)	<0.001	971 (3.9)	1575 (1.3)	1.91 (1.70–2.15)	<0.001
Disturbances of cognition and orientation	R41	54 (0.2)	80 (0.1)	1.82 (1.20–2.78)	0.013	21 (0.1)	48 (0.0)	1.11 (0.65–1.88)	0.748
Dizziness	R42	659 (2.6)	1358 (1.1)	1.45 (1.26–1.66)	<0.001	473 (1.9)	1032 (0.8)	1.33 (1.12–1.59)	0.003
Palpitations	R00.2	112 (0.4)	211 (0.2)	1.50 (1.13–2.00)	0.014	74 (0.3)	147 (0.1)	1.63 (1.19–2.24)	0.007
Chest pain	R07	443 (1.8)	1210 (1.0)	1.15 (0.97–1.38)	0.177	364 (1.5)	1021 (0.8)	1.06 (0.90–1.25)	0.561
Dyspnoea	R06	335 (1.3)	857 (0.7)	1.15 (0.92–1.43)	0.294	271 (1.1)	638 (0.5)	1.21 (0.99–1.47)	0.096
Hyperhidrosis	R61	62 (0.2)	134 (0.1)	1.27 (0.92–1.77)	0.213	50 (0.2)	114 (0.1)	1.30 (0.88–1.93)	0.258
Changes in appetite or weight	R63	160 (0.6)	366 (0.3)	1.28 (0.93–1.76)	0.201	121 (0.5)	264 (0.2)	1.41 (1.03–1.93)	0.057
Disturbances of skin sensation	R20	143 (0.6)	365 (0.3)	1.16 (0.87–1.55)	0.412	122 (0.5)	262 (0.2)	1.52 (1.19–1.94)	0.002
Nervousness and irritability	R45	386 (1.5)	576 (0.5)	1.46 (1.15–1.85)	0.005	256 (1.0)	440 (0.4)	1.40 (1.06–1.85)	0.039
Unspecific headache	R51	980 (3.9)	2314 (1.9)	1.27 (1.14–1.42)	<0.001	806 (3.2)	1873 (1.5)	1.30 (1.13–1.49)	<0.001
Abdominal pain, nausea	R10, R11	1381 (5.5)	4004 (3.2)	1.19 (1.05–1.34)	0.016	1239 (5.0)	3243 (2.6)	1.29 (1.15–1.46)	<0.001
Myalgia, fibromyalgia	M79	881 (3.5)	2240 (1.8)	1.28 (1.00–1.64)	0.083	756 (3.0)	1826 (1.5)	1.37 (1.07–1.74)	0.025
Joint pain	M25.5	507 (2.0)	1791 (1.4)	0.98 (0.85–1.14)	0.859	478 (1.9)	1489 (1.2)	1.07 (0.95–1.21)	0.350
Neck and shoulder complaints	M53, M75	844 (3.4)	2780 (2.2)	1.05 (0.94–1.18)	0.440	789 (3.2)	2420 (1.9)	1.13 (1.00–1.27)	0.076
Tension-type headache	G44.2	142 (0.6)	301 (0.2)	1.30 (1.03–1.66)	0.057	103 (0.4)	278 (0.2)	1.02 (0.76–1.37)	0.923
Migraine	G43	715 (2.9)	1603 (1.3)	1.54 (1.39–1.72)	<0.001	582 (2.3)	1346 (1.1)	1.46 (1.30–1.65)	<0.001
Irritable bowel syndrome	K58	119 (0.5)	265 (0.2)	1.25 (0.98–1.60)	0.111	101 (0.4)	225 (0.2)	1.35 (1.01–1.79)	0.072
Functional dyspepsia	K30	63 (0.3)	155 (0.1)	1.14 (0.80–1.63)	0.548	53 (0.2)	129 (0.1)	1.34 (0.92–1.94)	0.187
Gastritis	K29	906 (3.6)	3004 (2.4)	1.01 (0.86–1.17)	0.951	762 (3.1)	2558 (2.1)	0.95 (0.78–1.15)	0.650
Gastro-oesophageal reflux disease	K21	583 (2.3)	2067 (1.7)	0.93 (0.76–1.14)	0.569	564 (2.3)	1847 (1.5)	1.01 (0.83–1.23)	0.933
Constipation, functional intestinal disorders	K59	130 (0.5)	466 (0.4)	0.89 (0.69–1.14)	0.439	114 (0.5)	374 (0.3)	0.90 (0.67–1.22)	0.566

Table 4. *Cont.*

Diagnosis Group	ICD-10 Code(s)	Months 0–6 Before the Index Date				Months 6–12 Before the Index Date			
		Cases n (%)	Controls n (%)	OR (95% CI)	*p*-Value	Cases n (%)	Controls n (%)	OR (95% CI)	*p*-Value
Tinnitus	H93.1	267 (1.1)	439 (0.4)	1.77 (1.47–2.14)	<0.001	177 (0.7)	369 (0.3)	1.53 (1.25–1.87)	<0.001
Sudden hearing loss	H91.2	48 (0.2)	82 (0.1)	1.75 (1.15–2.65)	0.018	27 (0.1)	71 (0.1)	1.12 (0.67–1.87)	0.727
Acute respiratory tract infections	J00–J06, J20	5619 (22.5)	16,912 (13.6)	1.51 (1.42–1.60)	<0.001	5382 (21.6)	15,073 (12.1)	1.63 (1.53–1.74)	<0.001
Herpes labialis, herpes zoster	B00, B02	200 (0.8)	600 (0.5)	1.22 (1.03–1.46)	0.048	157 (0.6)	463 (0.4)	1.13 (0.93–1.36)	0.284
Urinary tract infections	N30, N39.0	547 (2.2)	2161 (1.7)	0.96 (0.85–1.08)	0.548	514 (2.1)	1734 (1.4)	1.09 (0.97–1.21)	0.204
Chronic skin diagnoses	L20, L40, L50, L63	305 (1.2)	982 (0.8)	1.08 (0.92–1.26)	0.445	273 (1.1)	808 (0.6)	1.20 (1.03–1.39)	0.040
Problems related to employment	Z56	330 (1.3)	262 (0.2)	2.94 (2.33–3.72)	<0.001	179 (0.7)	181 (0.1)	2.43 (1.86–3.19)	<0.001

OR, odds ratio; CI, confidence interval. Models were adjusted for sex, type of health insurance, age group, index year group, number of practice contacts, all diagnoses of interest, and 18 covariate diagnoses, with cluster-robust variance estimation at the practice level. *p*-values are corrected for the false discovery rate across all 76 tests. An FDR-adjusted *p*-value of less than 0.05 was considered statistically significant.

3.3. Proportion of Patients with Documented Symptom Diagnoses

At least one symptom diagnosis according to the broad definition was documented in 45.9% of cases and 26.2% of controls (OR 2.07; 95% CI 1.96–2.18) during the 6 months before the index date, and in 38.0% of cases and 21.7% of controls (OR 1.88; 95% CI 1.78–1.99) in the window covering months 6 to 12. For the exhaustion and stress complex, the corresponding proportions were 26.5% of cases and 9.6% of controls (OR 2.92; 95% CI 2.75–3.11) in the closer window, and 18.0% and 7.6% (OR 2.13; 95% CI 1.99–2.28) in the more distant window; for the conservative definition, 38.7% and 20.6% (OR 2.07; 95% CI 1.94–2.21) and 31.1% and 16.9% (OR 1.84; 95% CI 1.73–1.97), respectively (Figure 2). In separate models, each composite was associated with a subsequent burnout entry: ORs 2.07 (95% CI 1.96–2.18) for the broad definition, 2.92 (2.75–3.11) for the exhaustion and stress complex, and 2.07 (1.94–2.21) for the conservative definition in the closer window, and 1.88 (1.78–1.99), 2.13 (1.99–2.28), and 1.84 (1.73–1.97), respectively, in the more distant window (all $p < 0.001$). All three definitions therefore showed the same temporal pattern as the individual diagnoses, with the difference between cases and controls widening towards the index date, and the narrowest definition produced the strongest association. In absolute terms, however, the proportions remained moderate: in the six months preceding the burnout entry, no diagnosis from the exhaustion and stress complex had been documented in 73.5% of cases, and no symptom diagnosis of any kind in 54.1%.

Composite definitions. Broad definition: at least one of the following documented in the respective window: sleep disorders (G47, F51), depression (F32, F33), back pain (M54), reaction to severe stress and adjustment disorders (F43), other anxiety disorders (F41), somatoform disorders (F45), neurasthenia (F48.0), malaise and fatigue (R53), dizziness (R42), palpitations (R00.2), chest pain (R07), dyspnoea (R06), hyperhidrosis (R61), changes in appetite or weight (R63), disturbances of skin sensation (R20), nervousness and irritability (R45), unspecific headache (R51), abdominal pain or nausea (R10, R11), myalgia and fibromyalgia (M79), joint pain (M25.5), neck and shoulder complaints (M53, M75), tension-type headache (G44.2), migraine (G43), irritable bowel syndrome (K58), functional dyspepsia (K30), gastritis (K29), gastro-oesophageal reflux disease (K21), constipation or other functional intestinal disorders (K59), or herpes labialis and herpes zoster (B00, B02). Diagnoses that are not interpretable as a symptom presentation, that are largely defined by

the consultation itself, or that are conceptually adjacent to the burnout entry were excluded from this definition, namely the 18 covariate diagnoses, thyroid disorders, acute respiratory tract infections, urinary tract infections, chronic skin diagnoses, and problems related to employment.

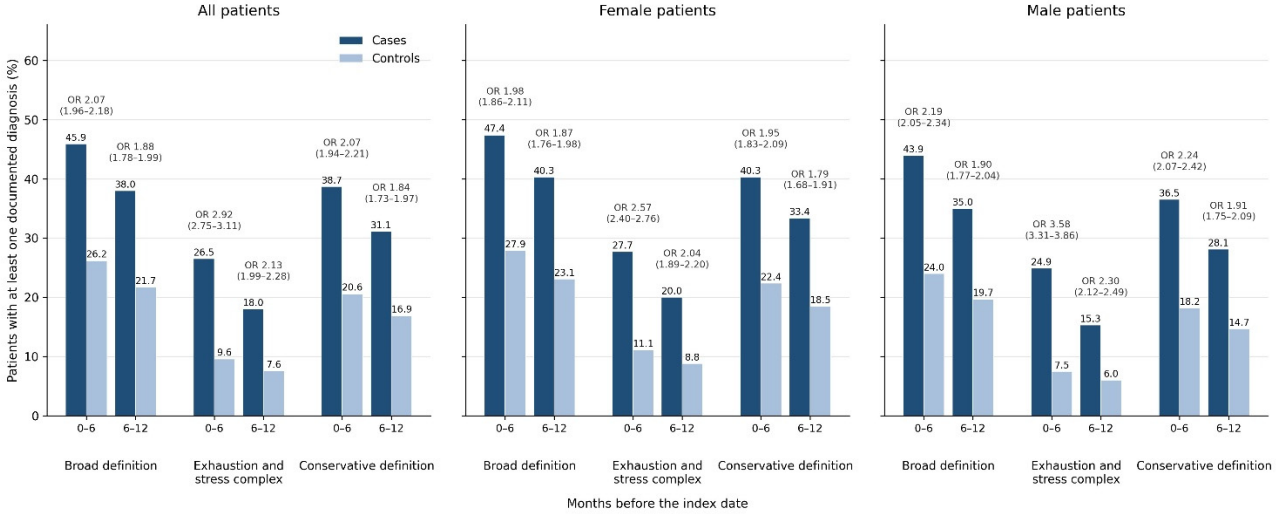


Figure 2. Proportion of patients with at least one documented diagnosis according to three composite definitions, by time window before the index date, for all patients and separately for female and male patients. Bars show the proportion of cases and of controls; the odds ratio with its 95% confidence interval above each pair is derived from a separate logistic regression model for the respective composite, adjusted for sex (in the overall panel), type of health insurance, age group, index year group, number of practice contacts within the window, and 18 covariate diagnoses, with cluster-robust variance estimation at the practice level.

Exhaustion and stress complex: at least one of neurasthenia (F48.0), malaise and fatigue (R53), reaction to severe stress and adjustment disorders (F43), sleep disorders (G47, F51), depression (F32, F33), somatoform disorders (F45), or other anxiety disorders (F41).

Conservative definition: the broad definition without depression (F32, F33) and without back pain (M54).

The number of distinct symptom diagnosis groups documented during the 6 months before the index date was zero in 54.1% of cases and 73.8% of controls, one in 21.9% and 16.2%, two in 12.2% and 6.1%, three in 6.3% and 2.4%, and four or more in 5.5% and 1.5%. The mean number of groups was 0.92 in cases and 0.43 in controls in the closer window, and 0.71 and 0.35 in the more distant window; the median was zero in all four groups.

3.4. Differences Between Male and Female Patients

Among female patients, at least one symptom diagnosis according to the broad definition was documented in 47.4% of cases and 27.9% of controls during the 6 months before the index date; among male patients, in 43.9% and 24.0%, respectively. For the exhaustion and stress complex, the proportions were 27.7% of cases and 11.1% of controls among female patients, and 24.9% and 7.5% among male patients. On the absolute scale, the difference between cases and controls was therefore almost identical in both sexes, at 19.5 versus 19.9 percentage points for the broad definition and 16.6 versus 17.4 percentage points for the exhaustion and stress complex in female versus male patients. The higher relative contrast among male patients reflects the lower proportion of symptom documentation among male controls rather than a more pronounced history among male cases. The mean number of documented symptom diagnosis groups in the closer window was 0.97 in female cases

versus 0.47 in female controls, and 0.86 in male cases versus 0.37 in male controls. Nevertheless, the corresponding ORs were higher in male patients for all three composite definitions, for example 3.58 (95% CI 3.31–3.86) versus 2.57 (2.40–2.76) for the exhaustion and stress complex in the closer window, and the interaction with sex was statistically significant for all three definitions in the closer window ($p < 0.001$, $p = 0.0003$, and $p = 0.012$) and for the exhaustion and stress complex in the more distant window ($p = 0.016$) (Figure 2).

In the models stratified by sex, point estimates were higher among male patients for most mental and functional diagnoses. After correction for multiple testing, formal evidence of effect modification was found for four of the 76 tests: malaise and fatigue in the closer window (OR 3.01 in male patients versus 2.13 in female patients), reaction to severe stress and adjustment disorders in the closer window (OR 2.46 versus 1.83), and gastro-oesophageal reflux disease in both windows, where the association was positive among male patients and inverse among female patients. For neurasthenia (OR 3.58 versus 2.54) and for neck and shoulder complaints, the difference did not reach the significance threshold after correction (Figure 3; Supplementary Table S1).

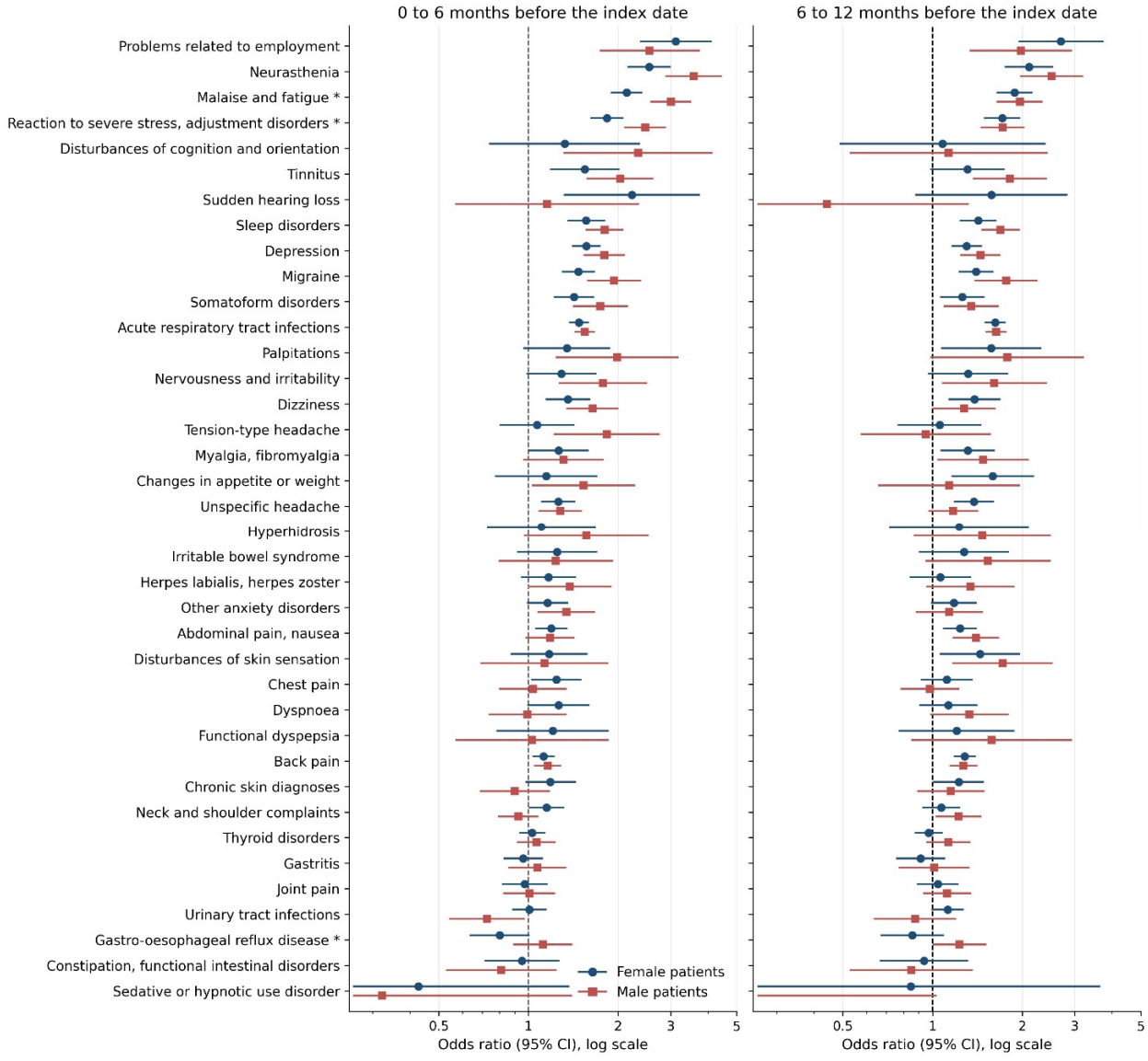


Figure 3. Odds ratios with 95% confidence intervals for each of the 38 diagnosis groups documented before the index date, estimated separately for female and male patients, by time window. The *x*-axis is on a logarithmic scale; two CIs extend beyond the plotted range and are truncated at the axis

limits (sudden hearing loss in male patients, 6 to 12 months; sedative or hypnotic use disorder, both windows). Diagnosis groups marked with an asterisk showed a statistically significant interaction with sex after correction for the false discovery rate. The corresponding numerical estimates, including the overall models and the interaction *p*-values, are given in Supplementary Table S1. The dashed vertical line indicates an odds ratio of 1.

3.5. Sensitivity and Additional Analyses

Repeating all models without adjustment for the number of practice contacts within the respective window changed the point estimates only marginally and did not alter any conclusion. Estimates were slightly higher without this adjustment, for example, 3.03 instead of 2.94 for problems related to employment and 2.47 instead of 2.39 for malaise and fatigue in the closer window.

In conditional logistic regression stratified by matched set, the ORs for problems related to employment, neurasthenia, malaise and fatigue, and reaction to severe stress in the closer window were 2.67 (95% CI 2.24–3.18), 3.01 (2.72–3.33), 2.32 (2.16–2.49), and 2.05 (1.92–2.20), respectively, compared with 2.94, 2.85, 2.39, and 2.02 in the main analysis. After FDR correction, 18 of the 38 diagnosis groups were significant in the closer window and 21 in the more distant window, compared with 20 and 19 in the main analysis. In the closer window, disturbances of cognition, sudden hearing loss, palpitations, and herpes infections were no longer significant, whereas myalgia and chest pain became significant. These differences reflect the wide CIs of rare diagnoses and the narrower CIs of the conditional model, which does not account for clustering within practices. Estimates for the composite definitions were virtually unchanged; for example, OR 2.94 (95% CI 2.83–3.05) for the exhaustion and stress complex in the closer window (Supplementary Table S2).

A documented COVID-19 diagnosis or post-COVID-19 condition before the index date was found in 4733 cases (19.0%) and 13,286 controls (10.7%), almost exclusively among patients with index dates from 2020 onwards. The OR for the exhaustion and stress complex in the closer window was 3.10 (95% CI 2.84–3.40) for index dates in 2005–2019, 2.89 (2.61–3.19) in 2020–2022, and 2.74 (2.52–2.98) in 2023–2025, and 3.05 (2.86–3.26) after excluding patients with a documented COVID-19 diagnosis or post-COVID-19 condition. Among the individual diagnoses, the association with malaise and fatigue in the closer window weakened over the three periods (OR 2.84, 2.44, and 2.03), whereas problems related to employment, neurasthenia, and reaction to severe stress were strongly associated with burnout documentation in all periods (Supplementary Table S3).

In the 6 months before the index date, antidepressants were prescribed to 7.4% of cases and 3.5% of controls (OR 1.58; 95% CI 1.43–1.74), hypnotics and sedatives to 3.4% and 1.2% (OR 2.04; 1.80–2.33), and tranquillisers to 1.5% and 0.7% (OR 1.28; 1.08–1.52). Non-steroidal anti-inflammatory drugs, analgesics, and antiulcerants were prescribed slightly more often to cases than to controls (11.6% versus 9.9%, 8.5% versus 7.3%, and 9.6% versus 7.9%), but after adjustment, these prescriptions were associated with lower odds of a subsequent burnout entry (ORs 0.89, 0.81, and 0.85) (Supplementary Table S4).

The c-statistic for the closer window was 0.612 (95% CI 0.609–0.616) for the model with matching variables and practice contacts, 0.614 (0.610–0.618) after adding the covariate diagnoses, and 0.646 (0.642–0.650) after adding all diagnoses of interest; the corresponding values for the more distant window were 0.610, 0.612, and 0.630. Considered as a single criterion, the exhaustion and stress complex in the 6 months before the index date had a sensitivity of 26.5% and a specificity of 90.4%, the broad definition 45.9% and 73.8%, and the conservative definition 38.7% and 79.4% (Supplementary Table S5).

The covariate diagnoses were mostly not positively associated with a subsequent burnout entry. In the closer window, the ORs were 1.03 (95% CI 0.95–1.12) for hypertension, 1.02 (0.91–1.13) for dyslipidaemia, and 1.00 (0.84–1.19) for obesity, whereas diabetes (OR

0.82; 0.71–0.94), cancer (0.48; 0.40–0.57), heart failure (0.65; 0.49–0.86), chronic kidney disease (0.72; 0.55–0.94), and epilepsy (0.52; 0.38–0.72) were inversely associated. The only positive association was observed for angina pectoris (OR 1.78; 1.31–2.42) (Supplementary Table S6).

4. Discussion

In this large, matched case–control study in German general practices, a first recorded burnout entry was preceded by a recognisable pattern of documented complaints. Problems related to employment, neurasthenia, malaise and fatigue, and reaction to severe stress showed the strongest associations, followed by sleep disorders, depression, somatoform disorders, and a range of functional and pain-related symptoms. These associations were markedly stronger in the 6 months immediately before the entry than in the preceding 6 months, whereas back pain and acute respiratory tract infections showed no such gradient. At the same time, the absolute proportions were modest: in the six months before the entry, no diagnosis from the exhaustion and stress complex had been documented in nearly three quarters of cases, and no symptom diagnosis of any kind in more than half.

The spectrum of complaints corresponds closely to what has been described in clinical populations. Patients presenting to specialised clinics with stress-related exhaustion report a heavy burden of somatic symptoms, with gastrointestinal complaints, headache, and dizziness among the most frequent (Glise et al., 2014), and all of these appear among the diagnoses associated with a subsequent burnout entry in our data. Reviews of clinical burnout and of exhaustion disorder describe sleep impairment and cognitive disturbance as core features of the condition rather than as comorbidities (Grossi et al., 2015; Lindsäter et al., 2022), which is consistent with the prominence of sleep disorders and of disturbances of cognition and orientation in the window closest to the entry. The association with sleep disorders also matches prospective evidence identifying insufficient sleep as a leading predictor of subsequent clinical burnout (Söderström et al., 2012). A retrospective chart review of 115 patients in Swedish primary care likewise found stress-related presenting complaints to be common in the two years before a diagnosis of exhaustion disorder (Adamsson & Bernhardsson, 2018). Our findings extend this observation in two respects: the complaints are more frequent than in matched individuals who did not receive a burnout entry, and they are not evenly distributed over the preceding year but concentrate close to the entry.

Several of the individual associations are biologically plausible in light of what is known about stress-sensitive conditions. Functional gastrointestinal disorders, including irritable bowel syndrome, are closely linked to psychological distress and are among the most common conditions in the general population (Ford et al., 2020; Sperber et al., 2021); migraine is frequently triggered and aggravated by stress and affects around one in ten people (Ashina et al., 2021); and tinnitus, which showed one of the higher ORs in our data, is highly prevalent and strongly associated with psychological burden (Jarach et al., 2022). Chronic stress acts on health through neuroendocrine, autonomic, and inflammatory pathways (O'Connor et al., 2021), and prospective studies have linked burnout to a broad range of subsequent somatic and occupational outcomes (Kivimäki & Steptoe, 2018; Salvagioni et al., 2017). The complaints we observed before the entry are therefore not a random selection of primary care diagnoses but correspond to the conditions in which a stress component is best established.

The temporal gradient deserves emphasis because it was largely confined to the exhaustion and stress complex. A general increase in documentation shortly before the index date could simply reflect more frequent consultations, and consultation frequency was indeed associated with burnout documentation. However, all models were adjusted for the number of contacts within the respective window, and the sensitivity analysis without

this adjustment changed the estimates only marginally. More importantly, the gradient was absent for back pain, which is a prominent occupational condition (Sabola et al., 2025) and for acute respiratory tract infections, which are documented at least as often as many of the diagnoses of interest and would be expected to rise in parallel with consultation frequency. The steepening pattern is therefore largely confined to the exhaustion and stress complex and is more compatible with an intensifying clinical presentation than with a general documentation artefact.

Temporal ordering, however, should not be mistaken for a causal sequence. A diagnosis documented before the burnout entry is not necessarily a cause of burnout. Several of the complaints, in particular fatigue, neurasthenia, sleep disturbance, and stress reactions, overlap with the core features of the syndrome itself (Grossi et al., 2015; Nadon et al., 2022) and may represent earlier manifestations of the same process that were documented under a different label before the burnout code was assigned. Others, such as migraine or tinnitus, may reflect a shared susceptibility to stress or a higher propensity to consult. The design identifies what is documented before the first record of burnout, not when the syndrome began or what caused it.

The study period included the COVID-19 pandemic, which is relevant for two reasons. Persistent fatigue and cognitive impairment are reported by a substantial proportion of individuals after COVID-19 (Ceban et al., 2022), so that post-COVID-19 complaints could have been coded as malaise, fatigue, or cognitive disturbance and later relabelled as burnout; at the same time, the pandemic increased occupational strain, particularly in health care, where about half of the workforce reported burnout during this period (Ghahramani et al., 2021). In our data, the associations were similar across the three index periods and after excluding patients with a documented COVID-19 diagnosis or post-COVID-19 condition, which argues against a substantial distortion of the results by the pandemic (Supplementary Table S3). The weaker association for malaise and fatigue in 2023–2025 is compatible with fatigue being documented more often for other reasons, including post-COVID-19 complaints, among controls in this period, and the higher proportion of cases with a documented COVID-19 diagnosis may partly reflect their higher consultation frequency. Post-COVID-19 condition may nevertheless have been underdocumented, particularly in the early phase of the pandemic, before a specific code was available.

The prescription data add information on the perceived severity of the documented complaints. Antidepressants, hypnotics and sedatives, and tranquillisers were prescribed considerably more often to cases than to controls in the months before the burnout entry, indicating that the mental and sleep-related complaints were frequently considered severe enough to warrant pharmacological treatment; greater burnout has also been associated with changes in prescribed psychotropic medication among healthcare workers in prescriber and administrator roles (Hoopsick et al., 2024). In contrast, analgesics, non-steroidal anti-inflammatory drugs, and antiulcerants were associated with lower odds of a subsequent burnout entry after adjustment, despite slightly higher crude proportions among cases. These drugs are mainly prescribed for somatic conditions, and the inverse adjusted associations suggest that, once consultation frequency and covariate diagnoses are taken into account, such prescriptions mark somatic morbidity rather than the stress-related process preceding the burnout entry.

The second main finding points in the opposite direction and is equally important. For most patients, the burnout entry appears in the record without any documented antecedent. Two interpretations are possible, and both are relevant for care. Patients may genuinely present late, consulting only when exhaustion has reached a point at which it cannot be compensated any longer; in that case, the problem lies with the pathway into care, and with the threshold at which occupational strain is brought to a physician at all. Alternatively,

the complaints may have been voiced and addressed but not coded, which is plausible in German outpatient documentation, where coding follows the reason for the encounter, with a somatic principal diagnosis absorbing the consultation. The under-recognition of medically unexplained and somatoform presentations in primary care is well described (Haller et al., 2015) and would affect the results in the same direction. Our design cannot distinguish between these explanations. What it does establish, however, is a boundary condition: whichever explanation holds, routine primary care data contain a documented antecedent for only a minority of patients, and expectations of what such data can achieve for early identification or for algorithm-based risk stratification should be calibrated accordingly. This is also reflected in the limited discriminative ability of the documented diagnoses: even the exhaustion and stress complex identified only about one quarter of cases, and adding all diagnoses of interest to a model with matching variables and practice contacts increased the c-statistic only from 0.612 to 0.646 (Supplementary Table S5).

For general practice, the findings suggest that recurrent consultations for exhaustion, fatigue, sleep disturbance, nervousness, or stress reactions, particularly when they accumulate within a few months, may be a reasonable occasion to ask explicitly about the patient's working situation. Such questions require no diagnostic instrument and may help to distinguish a work-related exhaustion process from other causes of fatigue. Because most patients had no such diagnosis before the burnout entry, however, relying on diagnostic records alone would miss the majority of them. Moreover, the early recognition of stress-related complaints in individual patients is not the same as the prevention of occupational burnout: longitudinal evidence indicates that burnout symptoms are strongly associated with job demands, job control, and workplace support (Aronsson et al., 2017), so that prevention also requires attention to psychosocial working conditions at the level of employers and organisations. At the policy level, our results argue for more systematic documentation rather than for new diagnostic categories. Z codes describing psychosocial and occupational problems are used sparingly in routine care in other health systems (Truong et al., 2020), and in our study the code for problems related to employment was documented in only 1.3% of cases in the six months before the burnout entry. Encouraging the recording of occupational strain alongside symptom diagnoses could improve continuity of care and the usefulness of routine data for research.

The comparison between female and male patients illustrates how misleading the multiplicative scale can be in this setting. Relative contrasts were larger in male patients for most mental and functional diagnoses, and the formal test of effect modification reached significance for malaise and fatigue and for reaction to severe stress. On the absolute scale, however, the difference between cases and controls was almost identical in both sexes, with around 17 percentage points for the exhaustion and stress complex and around 20 percentage points for the broad definition. The larger relative contrast in male patients is a consequence of the lower level of symptom documentation among male controls, which is consistent with the well-described sex difference in consultation and documentation behaviour, rather than evidence that male cases had more complaints documented before the burnout entry than female cases. We therefore interpret the sex comparison as showing a comparable increment in both sexes on a different baseline.

Two of the diagnoses examined require separate comment. Problems related to employment yielded the highest odds ratio, but this code is conceptually adjacent to the burnout entry itself and is likely to be assigned by the same physician working from the same interpretation of the patient's situation. Although the index day was excluded from all windows, the association should be read as evidence that the occupational framing precedes the formal entry, not as an independent risk marker. Acute respiratory tract infections, on the other hand, are close to contact-defined: they are among the most common reasons

for a consultation and therefore present an opportunity for any further documentation. They are reported for completeness but should not be interpreted as complaints related to the burnout process. Depression occupies an intermediate position: given the substantial, though incomplete, overlap between burnout and depressive symptoms (Koutsimani et al., 2019), a documented depressive episode preceding a burnout entry may represent an earlier attempt to name the same clinical picture rather than a distinct antecedent condition.

The distinction between diagnoses of interest and covariate diagnoses also requires comment, because many of the covariate conditions are themselves related to stress and mood (Graham et al., 2020; Kivimäki & Steptoe, 2018; Liu et al., 2017). Our classification therefore does not imply that these conditions are unrelated to stress; it reflects the time frame of the study. Within 12 months before a burnout entry, a symptom-based diagnosis such as irritable bowel syndrome, dyspepsia, or sleep disturbance can reflect a current complaint, whereas chronic cardiometabolic, renal, neurological, and malignant diseases develop over years and, once diagnosed, are documented repeatedly, so that their presence in a 6-month window mainly marks long-standing morbidity. Consistent with this, the covariate diagnoses were largely unrelated or inversely related to a subsequent burnout entry, and adding them to the model increased the c-statistic by only 0.002 (Supplementary Tables S5 and S6). The inverse associations may reflect that consultations of patients with severe chronic disease are dominated by that disease and that these patients are less often in active employment, whereas the positive association for angina pectoris is compatible with stress-related chest complaints being coded as angina. Whether occupational stress contributes to the long-term development of these chronic conditions is a separate question, which our design with its 12-month window was not intended to answer.

The findings also bear on the debate about whether burnout should be regarded as a medical or psychiatric condition or as a condition of employment. ICD-11 classifies burnout as an occupational phenomenon, and a recent review concluded that introducing it as a distinct mental disorder would be premature (Nadon et al., 2022). In routine care, the burnout code was preceded by diagnoses of depression, anxiety, somatoform disorders, and neurasthenia, as well as by somatic complaints. This is consistent with the psychobiological alterations described in clinical burnout (Bayes et al., 2021). At the same time, the preceding documentation of problems related to employment shows that the occupational context is part of how physicians frame the condition. Our data cannot resolve this debate, but they suggest that in German general practice, burnout functions as an interface between medical care and occupational health, which supports approaches that combine clinical management of symptoms with attention to working conditions.

Because no information on occupation was available, the findings cannot be related to specific occupational groups. Internationally, burnout has been studied most extensively in the health sector: a meta-analysis of 61 studies from 49 countries estimated a pooled prevalence of burnout symptoms among nurses of 11.2%, with the highest prevalence in sub-Saharan Africa and the lowest in Europe and Central Asia (Woo et al., 2020), and among primary health care professionals in low- and middle-income countries, 28.1% had a high level of emotional exhaustion (Wright et al., 2022). During the COVID-19 pandemic, the prevalence of burnout among healthcare workers differed between countries of different income levels (Ghahramani et al., 2021). Comparisons between high-income and low- and middle-income countries are limited by heterogeneous instruments and definitions (Edú-Valsania et al., 2022) and, more fundamentally, by the fact that burnout is documented in medical records mainly in settings such as Germany, where burnout is an accepted reason for consultation and sick leave is certified by physicians (Kostev et al., 2024). In many low- and middle-income countries, occupational burnout is captured predominantly by surveys

of specific professional groups, so the documentation pathway examined here is unlikely to be transferable to these settings.

The strengths of this study include its size, the use of nationwide primary care data that are broadly representative of German general practice (Kostev et al., 2026; Rathmann et al., 2018), exact matching on the principal structural confounders, adjustment for consultation frequency, a sensitivity analysis using conditional logistic regression, cluster-robust estimation at the practice level, and correction for multiple testing across a pre-specified set of diagnoses. Several limitations should be acknowledged. Firstly, in WHO ICD-10, burnout is not a disease entity in its own right, but a code within a supplementary chapter (World Health Organization, 2019), and no consensual diagnostic criteria exist (Edú-Valsania et al., 2022; Maslach & Leiter, 2016); cases are therefore defined by physician documentation behaviour as much as by patient condition. In ICD-10 German Modification, the chapter Z73 (entitled Problems related to difficulties coping with everyday life) includes psychosocial problems other than burnout (Bundesinstitut für Arzneimittel und Medizinprodukte, 2026), although states of exhaustion did account for over 80% of the free-text entries associated with the Z73.0 diagnoses. Moreover, it could not be verified whether patients exhibited the characteristic dimensions of burnout, were in paid employment, or had been exposed to chronic occupational stress, so the findings may not be generalisable to workers in whom burnout is identified by clinical criteria or standardised instruments (Maslach & Leiter, 2016). The index date also marks the first documentation of burnout, not the onset of the syndrome, which may have begun considerably earlier. Secondly, only diagnoses documented in the contributing general practices were available, so complaints addressed by specialists, in hospitals, or in psychotherapeutic care are not captured, and controls may include individuals whose burnout was recorded elsewhere. Specialist diagnoses preceding the burnout entry may likewise be missing from the analysed dataset. Thirdly, no information was available on occupation, working conditions, sick leave, or the severity of complaints, so that specific occupational groups such as healthcare workers could not be identified, and residual confounding cannot be excluded. Prescriptions were used as an indirect indicator of severity, but they capture only drugs prescribed in the practice and not over-the-counter medication or prescriptions issued elsewhere. Fourthly, the index date of controls was a randomly selected visit date, which is an arbitrary, although pragmatically reasonable, anchor. Finally, the study design is observational and identifies associations in documentation rather than causal relationships.

5. Conclusions

In conclusion, in this study of adults treated in German general practices, a first recorded burnout diagnosis was preceded by a pattern of documented complaints that concentrated in the final six months and centred on exhaustion, stress reactions, sleep disturbance, and functional symptoms. These findings concern patterns of clinical documentation preceding the first recorded burnout diagnosis and should not be interpreted as validated early indicators of the syndrome, because neither working conditions nor the specificity of these complaints for burnout compared with other conditions were assessed. For most patients, however, no such antecedent was recorded in the six months before the burnout entry. Recurrent exhaustion- and stress-related complaints may nevertheless be a reasonable occasion for general practitioners to ask about the patient's working situation, whereas the prevention of occupational burnout requires attention to psychosocial working conditions beyond primary care.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/ejihpe16120185/s1; Table S1: Associations between diagnoses documented before the index date and burnout documentation, overall and separately for women and men; Table S2: Associations between diagnoses documented before the index date and burnout documentation: main analysis compared with conditional logistic regression; Table S3: Associations between diagnoses documented before the index date and burnout documentation by index period and after exclusion of patients with a documented COVID-19 diagnosis or post-COVID-19 condition; Table S4: Prescriptions documented before the index date in cases and controls; Table S5: Discrimination of the documented diagnoses between cases and controls; Table S6: Associations between covariate diagnoses documented before the index date and burnout documentation.

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Institutional Review Board Statement: This study used data from the Disease Analyzer database. This data is relatively anonymous. This assessment is based on the relative anonymity concept, as can be seen from Recital 26 GDPR and the ECJ decision (judgement of 26 April 2023–T-557/20). In the data sets made available to IQVIA, the personal references have been removed by third parties as trustees or by software-supported measures in the doctors' practices, by encryption, so that re-identification by IQVIA is practically impossible. According to the EU General Data Protection Regulation (GDPR, Recital 26) and the German Federal Data Protection Act (Bundesdatenschutzgesetz, BDSG § 27), research using anonymous data does not involve identifiable individuals and therefore does not require informed consent or approval by an ethics committee. As no directly or indirectly identifiable data were available to the authors at any time, ethics approval was not required for this observational study.

Informed Consent Statement: Patient consent was waived because the study was based exclusively on anonymized electronic medical records that contain no directly identifiable data.

Data Availability Statement: The data were obtained from the Disease Analyzer database (IQVIA) and are not publicly available; access for scientific purposes is subject to a licence agreement with IQVIA. The data used in this study cannot be made available in the manuscript, the tables, or the Supplementary Materials due to data protection laws.

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Abbreviations

The following abbreviations are used in this manuscript:

CI	Confidence interval
COVID-19	Coronavirus disease 2019
EphMRA	European Pharmaceutical Market Research Association
FDR	False discovery rate
ICD-10	International Classification of Diseases, 10th revision
ICD-10-GM	ICD-10, German Modification
ICD-11	International Classification of Diseases, 11th revision
OR	Odds ratio
WHO	World Health Organization

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