

1 Burden of psychiatric and somatic comorbidities in
2 individuals with suicidal behavior: A nationwide Danish
3 registry-based, observational study

4 **Short title:** Comorbidity burden and suicidal behavior

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17 Abstract

18

19 *Background*

20 A range of single psychiatric and somatic comorbidities increase the risk of suicidal behavior, but the
21 effect of co-existing comorbidities is sparsely elucidated. We described co-existence of psychiatric and
22 somatic comorbidities, and the influence of the combined comorbidity burden on the risk of suicidal
23 behavior.

24 *Methods*

25 We defined two case populations above 10 years in the Danish health registries: those who 1) died by
26 suicide (2010-2020) and 2) had an incident suicide attempt (2010-2021). Co-existing somatic and
27 psychiatric comorbidities and relative odds of suicidal behavior at increasing comorbidity burden were
28 assessed.

29 *Results*

30 Among 5.9 million Danish citizens (2021), 6,257 individuals died by suicide whereas 30,570 had an
31 incident suicide attempt. More than half had ≥ 2 co-existing psychiatric and/or somatic comorbidities.
32 Of those who died by suicide, 18% had co-existing mood disorders and stress disorders, while 5% had
33 both mood disorders and cancer. An 88-fold increase of odds for attempting suicide and a 35-fold
34 increase of odds for suicide were observed among those with the highest combined burden of somatic
35 and psychiatric comorbidities relative to those without. The presence of somatic comorbidities seemed
36 to protect against suicide in older individuals.

37 *Conclusions*

38 Psychiatric and somatic comorbidities commonly co-exist in individuals with suicidal behavior. Higher
39 combined burden of psychiatric and somatic comorbidities increased the odds of suicidal behavior,
40 though the presence of somatic diseases had a potential protective effect on the risk of suicide in older
41 individuals. This warrants collaboration and enhanced awareness of suicidal behavior risks across
42 somatic and psychiatric departments.

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45 Introduction

46 The identification of individuals at high risk of suicidal behavior stands as a paramount imperative in
47 public health and clinical practice to prevent suicide [1]. Despite extensive research efforts, it is difficult
48 to distinguish those who act on suicidal thoughts from those who do not and simple suicide risk
49 assessment models including single risk factors are deemed inadequate. This is partly due to the
50 complex nature of suicide with intricate dynamic interactions between social, psychological, and
51 biological determinants [2], and partly due to the low base rates of suicidal behavior. An extensive
52 meta-analysis including the last 50 years of research in suicidal behavior evaluated the value of risk
53 assessments and found that no single risk factors seem to hold a substantial clinical value if evaluated
54 separately. Instead, a nuanced exploration of the interplay between several risk factors is needed to
55 augment the clinical value [3].

56 A range of isolated psychiatric disorders and somatic diseases are known to increase the risk of suicidal
57 behavior. To this end, individuals with psychiatric disorders like psychotic disorders and mood
58 disorders have a many fold higher risk of suicide (RR 12-13), but also for some somatic diseases like
59 epilepsy and concussion, the risk of suicide is correspondingly increased 2-3-fold [4]. Despite this,
60 there is a paucity of studies evaluating whether co-existence of psychiatric and somatic comorbidities
61 increases the risk of suicide to a magnitude relevant for risk assessment in clinical practice.

62 To adopt the most comprehensive and informative approach for risk assessment, detailed knowledge
63 about co-existing somatic and psychiatric comorbidities in individuals with suicidal behavior is
64 mandatory. In this study, we therefore aimed to map prevalence and co-existence of psychiatric
65 disorders and somatic diseases in individuals with suicidal behavior, and to determine whether the
66 combined burden of somatic and psychiatric comorbidities affects the risk of suicide and suicide
67 attempt.

68 Methods

69 In this nationwide, registry-based, descriptive study, we described co-existence and burden of
70 psychiatric disorders and somatic diseases among all Danish individuals above 10 years of age with
71 suicidal behavior from 2010-2021.

72 *Data sources*

73 The entire Danish population has access to tax funded healthcare services regardless of age, sex, and
74 income. This includes free access to both primary and secondary care. The National Health Service
75 System stores individual-level information on provided healthcare services in nationwide health
76 registries.

77 Through the unique personal identifier provided to all Danish citizens [5], data from the nationwide
78 health registries were linked to individual-level data on income, civil status, etc. from Statistics

79 Denmark. The following four health registries were used: the Danish National Patient Registry, the
80 National Prescription Registry, the Danish Civil Person Registry, and the Causes of Death Registry.

81 The Danish National Patient Registry covers data on e.g., date of admission and the discharge
82 diagnoses coded by the International Classification of Disease 10th version (ICD-10) [6] for all hospital
83 admissions since 1977 and contacts to outpatient clinics and psychiatric wards since 1995. The National

84 Prescription Registry records data on all redeemed prescription drugs by Danish citizens at outpatient
85 pharmacies since 1995 and onward [7]. Among others, prescription data include the date of dispensing
86 and the substance. Drugs are categorized according to the Anatomical Therapeutic Chemical (ATC)

87 code, developed by the WHO for purposes of drug use statistics [8]. The Danish Civil Person Registry
88 covers every Danish citizen and records data on vital status (date of birth and death) and migrations to

89 and from Denmark [5]. The Danish Register of Causes of Death contains information on the date,
90 cause, and mode of death (natural cause, suicide, homicide, or accident) [9].

91 *Study population*

92 Case- and reference groups were built separately for each outcome. The case groups included all
93 Danish citizens who had an incident suicide attempt from 1 January 2010 to 31 December 2021, and a
94 suicide from 1 January 2010 to 31 December 2020. Due to shorter lag time in the Danish National than
95 in the Cause of Death Registry Patient Registry, more recent data were included in the analysis of
96 suicide attempts. To inform the reader of prevalences and co-existences of comorbidities in similar
97 groups of individuals in the background population, we established reference groups including
98 individuals who had not (yet) experienced the outcome by matching in a ratio of 1:10 on age, sex, at the
99 index dates of the corresponding cases. Individuals in the reference groups were assigned an index date
100 identical to the outcome date of the corresponding case. To be included, individuals in the case- and
101 reference groups were at least 10 years old at the outcome-/index date. Individuals were excluded if
102 data source coverage was incomplete during a 10-year window prior to the outcome-/index date.

103 *Definition of suicide and suicide attempt*

104 Two outcomes were considered: 1) suicide and 2) incident suicide attempt. Incident suicide attempt was
105 defined as the first recording of diagnosis codes indicating deliberate self-harm using a 10-year
106 lookback. Acknowledging that some misclassification of suicide attempts may occur [10], a broader
107 definition of suicide attempts was applied in a sensitivity analysis. In addition to deliberate self-harm,
108 this definition also covered events of undetermined intent, accidental poisonings, and injuries to the
109 lower forearm in individuals diagnosed with psychiatric disorders. A detailed description of coding
110 algorithms used to define outcomes can be found in **e-Table 1**.

111 *Definition of psychiatric and somatic comorbidities*

112 The most common and/or severe chronic somatic diseases and psychiatric disorders were selected *a*
113 *priori* by the author group. For a complete list hereof including corresponding coding algorithms, see **e-**

114 **Table 2.** A 10-year lookback in the health registries was used to establish the existence of a disease.
115 Only these prespecified diseases were included in the analyses described below. Throughout the paper,
116 “co-existing comorbidities” refers to the recording of two or more somatic diseases and/or psychiatric
117 disorders in the Danish National Patient Registry during this 10-year lookback period.

118 *Statistical analysis*

119 Individuals were characterized on the outcome-/index date in terms of sex, age, socio-economic
120 factors, and history of somatic diseases and psychiatric disorders and hospital admissions.

121 Next, the 10 most common psychiatric disorders and somatic diseases and co-existence hereof were
122 illustrated in a network graph, where the size of the nodes is proportional to the number of individuals
123 with a given disease and the thickness of the links between the nodes to the number of individuals
124 sharing both diseases. To avoid over-cluttering of the network graph, only diseases co-existing in more
125 than 1% of individuals were visually linked to each other.

126 Finally, the crude odds ratios (ORs) of suicidal behavior given different burdens of psychiatric and
127 somatic comorbidities on the outcome-/index date were visualized in a heat map with the count of
128 somatic diseases (0, 1, 2, 3+) on the x-axis and the count of psychiatric disorders (0, 1, 2, 3+) on the y-
129 axis. For each cell in the heat map, the odds for experiencing the outcome when having a specific
130 combination of counts of psychiatric and somatic comorbidities was determined and the odds for
131 experiencing the outcome when having zero somatic diseases and zero psychiatric diseases was used as
132 reference, thus providing crude ORs. Crude ORs were calculated using conditional logistic regression,
133 and can in this case be interpreted as risk ratios, since the outcome is rare and controls are drawn from
134 the background population [11]. Each disease contributed in an unweighted manner, i.e., ignoring that
135 different diseases add differently to the risk of suicidal behavior. *Post hoc*, it was estimated whether the
136 existence of somatic diseases (yes/no) modified the relative odds of experiencing the outcome if having

137 0, 1, or 2+ psychiatric diseases by including somatic diseases, psychiatric disorders, and the
138 combination hereof as an interaction term.

139 All analyses were performed for the overall case- and reference groups built for each outcome.

140 Analyses were repeated stratified by sex. For suicide attempts, a sensitivity analysis was conducted
141 based on the broader definition hereof (see *Outcomes*).

142 *Other*

143 According to Danish law, studies based entirely on registry data do not require approval from an ethics
144 review board.[12] The study was registered at the repository of the University of Southern Denmark
145 (notification number 11.773) and data were available from Statistics Denmark (project number 708951).
146 Due to legal reasons, individual-level data cannot be shared by the authors.

147 Results

148 In a population of 5.8 million Danish citizens (2020), 6,257 individuals died by suicide from 2010-2020
149 whereas 30,570 had a first suicide attempt from 2010-2021. Those who died by suicide were more often
150 men (73% vs. 40% among individuals who attempted suicide) and older (median age 55 years vs. 31
151 years for individuals who attempted suicide) (Error! Reference source not found.).

152 Both among individuals who died by suicide and among those who attempted suicide, hospital
153 admission rates at psychiatric and somatic departments were higher than in the reference groups. E.g.,
154 in the month leading up to the suicide, 7.7% had been admitted to a psychiatric department while 14%
155 had been admitted to a somatic department compared to 0.1% and 1.3% in the reference group (Error!
156 Reference source not found.).

157 Across outcomes, the prevalence of single psychiatric comorbidities was high and largely similar as
158 illustrated by the size of the nodes in the network graph (**Figure 1**). Mood disorders were most
159 common (recorded in approximately half of individuals in both case groups) followed by other stress

160 disorders than PTSD (23% of those who died by suicide vs. 30% of those who had their first suicide
161 attempt), and alcohol abuse (22% of those who died by suicide vs. 21% of those who had their first
162 suicide attempt). In terms of single somatic diseases, minor differences were observed across outcomes.
163 To this end, cancer and ischemic heart disease were the most prevalent single somatic diseases in those
164 who died by suicide (10% vs. 9%), while traumatic brain injury and chronic lung disease occurred most
165 frequently among those who attempted suicide (9% vs. 8%) (**Figure 1**). Irrespective of outcome, co-
166 existence of psychiatric diseases was common as illustrated by the thickness of the links between nodes
167 in the network graph. More than half (55% vs. 56%) had two or more co-existing psychiatric and/or
168 somatic diseases. Most frequently, mood disorders and other stress disorders co-existed in 18% of
169 individuals who died by suicide and in 19% of those who had their first suicide attempt. Among the
170 most frequent combinations of psychiatric disorders and somatic diseases were mood disorders and
171 cancer (4.8% of those who died by suicide), and mood disorders and traumatic brain injury (4.5% of
172 those who attempted suicide) (**Figure 1**). For both outcomes, the prevalence of psychiatric disorders
173 and somatic diseases, alone or in combination, was several folds higher than in the reference groups (**e-**
174 **Figure 2**). Sex stratified analyses revealed important differences, particularly among those who died by
175 suicide. To this end, the prevalences of the most frequent psychiatric disorders were higher among
176 women, e.g., 66% of women who died by suicide had a diagnosis of mood disorders compared to 43%
177 of men (**e-Table 3**).

178 When investigating the association between the burden of comorbidities, we found generally increasing
179 relative odds of attempting suicide the higher the combined burden of somatic and psychiatric disease.
180 To this end, the odds of attempting suicide was 88-fold higher among those who had three or more
181 psychiatric and somatic comorbidities relative to those who had zero comorbidities (**Figure 2**).
182 Similarly, the odds of dying by suicide was 35-fold higher among those with three or more psychiatric
183 and somatic comorbidities. The burden of somatic diseases did, however, not seem to augment the
184 association as observed among those who attempted suicide (**Figure 2**). The observed increase in

185 relative odds of suicide and suicide attempt was evident for both sexes, though most pronounced for
186 women who died by suicide (**e-figure 3**). This potential modifying effect of somatic diseases on the risk
187 of suicide was further investigated in a *post hoc* analysis. We found a slightly lower crude OR in
188 individuals with at least one somatic disease, e.g., if having two psychiatric diseases, the crude OR was
189 14 if having at least one somatic disease while the crude OR was 18 in the absence of somatic diseases.
190 Stratifying by age groups, the presence of somatic diseases seemed to have a protective effect in
191 individuals older than 40 years (e.g., crude OR 18 if zero somatic diseases and 2 psychiatric diseases vs.
192 crude OR 12 in the presence of somatic disease), whereas the opposite pattern emerged for young
193 adults (**Table 2**).

194 Acknowledging some level of misclassification of suicide attempts in the Danish health care registries,
195 we applied a less restrictive definition of suicide attempts in a sensitivity analysis. This revealed more
196 conservative findings, e.g., a lower proportion of women, less prevalent psychiatric disorders, and lower
197 crude ORs of the combined burden of psychiatric and somatic comorbidities, though the general
198 tendencies remained unchanged (data not shown).

199 Discussion

200 In this observational study, we mapped co-existence of the most prevalent psychiatric and somatic
201 diseases and estimated the influence of the increasing burden of psychiatric and somatic comorbidities
202 on the risk of having suicidal behavior. We found that more than half of individuals with suicidal
203 behavior had at least two co-existing psychiatric and/or somatic diseases, most commonly psychiatric
204 disorders like mood disorders and stress disorders, and somatic disorders like cancer and traumatic
205 brain injury. We also found higher relative odds of suicidal behavior the higher the combined burden of
206 somatic and psychiatric comorbidities. *Post hoc* analysis revealed, however, a potential protective effect
207 of the presence of somatic diseases on the risk of dying by suicide in the older age groups.

208 *Strengths and limitations*

209 The Danish healthcare registries cover data on hospital admissions and drug use on all Danish citizens
210 irrespective of age, sex, and income. This provides unique opportunities to perform observational,
211 population-based suicide research on high-quality data covering an entire nation. Of note, the registries
212 are built for administrative purposes, and limitations should be considered, mainly related to
213 misclassification of outcomes and variables. Misclassification of suicide is minimal in the Danish Cause
214 of Death registry [13]. For suicide attempts, some misclassification is known to occur. The most
215 restrictive definition used in the main analysis has a positive predictive value of 73% [10], and is widely
216 accepted in Danish registry-based suicide research. Differential misclassification may occur, i.e., that
217 suicidal behavior is more likely to be registered as such in individuals with existing psychiatric diseases.
218 This would overestimate the crude ORs illustrated in the heat map, though unlikely to an extent that
219 explains the magnitude of the crude ORs observed in this study. Similarly, it cannot be ruled out that
220 suicidal behavior is more likely to be registered as such if the number of somatic diseases increases. If
221 such misclassification is present, our estimates are conservative of the potential protective effect of
222 somatic diseases on suicide risk among the oldest.

223 The completeness of recordings in the health registries is generally good, and the recording of deaths in
224 the Cause of Death registry is complete.[9]. Some under-recording of suicide attempts is known to
225 occur. Individuals who do not seek medical attention following a suicide attempt are not covered or
226 might be incorrectly registered as having had an accident or another illness. Some reluctance towards
227 properly registering suicidal attempt as the cause of contact exists [14], i.e., suicidal attempts might be
228 recorded as a drug overdose or accident. To meet this, we did a sensitivity analysis using less restrictive
229 definitions including certain codes indicating drug overdose or accidents. This led to more conservative
230 crude estimates of OR related to the combined burden of comorbidities likely indicating some washout
231 of the results due to a higher level of misclassification. While the recording of chronic diseases like

232 diabetes or epilepsy, that requires specific medical treatment or intervention in the hospital is close to
233 complete, other less abruptly occurring chronic diseases like obesity or mild depression may be under-
234 recorded. As such, this study presents a conservative estimate of the co-existence of diseases, which in
235 reality is probably aggravated even further in psychiatric patients in whom somatic diseases are
236 underdiagnosed [15].

237 *Comparison with existing literature*

238 The combined burden of co-existing mental disorders and physical illnesses in individuals with suicidal
239 behavior is sparsely elucidated in existing literature. Indirectly supporting the validity of our results is
240 the previously observed high prevalences of mental disorders and physical illnesses when evaluated
241 separately. In accordance with our findings, a meta-analysis suggests that mental disorders are present
242 in up to 71% of 35-65-year-olds who die by suicide [16], while a case-control study from the US found
243 that physical illnesses were present in 62% of those who died by suicide. In addition, they found that
244 physical multimorbidity (2 or more conditions) was associated with a 4-fold increase in the risk of
245 suicide [17]. As isolated risk factors, physical illnesses like cancer, stroke, and COPD also seem to
246 increase the risk of suicidal behavior [17–20] though less than mental disorders like major depressive
247 disorders and bipolar diseases, where the risk of suicide is increased up to 9-fold [21].

248 In the present study, an 88-fold increase in the odds of suicide attempt and a 35-fold increase in the
249 odds of suicide was observed among individuals who had 3 or more of both psychiatric and somatic
250 comorbidities relative to those who had none. This has not been shown before but is indirectly
251 supported by a study indicating that suicide risk was particularly elevated if somatic diseases and
252 psychiatric disorders were diagnosed close in time to each other [22]. Altogether, this indicates that the
253 combined burden of disease is an important measure in the prediction of suicidal behavior. It is,
254 however, puzzling that the presence of somatic diseases seems to have a potentially protective effect on
255 the risk of suicide in the oldest age groups, though the same cannot be found for suicide attempts.

256 *Clinical implications and future perspectives*

257 The high prevalences of psychiatric and somatic comorbidities observed in this study underpins that
258 these are important components in suicide risk algorithms, particularly if being present at the same
259 time. The preventive potential hereof should be investigated, for example through calculations of
260 absolute risk increases and attributable proportions related to the most frequent combinations of
261 psychiatric and somatic diseases, e.g., mood disorders and cancer in the oldest, and mood disorders and
262 traumatic brain injury in the younger age groups. From a clinical perspective, our results emphasize the
263 need for enhanced awareness of suicidal risk across both somatic and psychiatric departments and
264 suggest that close collaborations between psychiatric and somatic departments as well as across primary
265 and secondary care is warranted to prevent suicidal behavior.

266 The ambiguous finding that somatic diseases potentially protect against suicide in the oldest
267 multimorbid patient is of interest. This might indicate a collateral benefit of the more intensive health
268 care and treatment demanded by those with a higher burden of somatic diseases. An alternative
269 explanation is that older individuals with a high burden of disease and functional impairment are taken
270 care of at nursing home facilities. Since nursing homes permit 24-hour care and frequent interventions
271 between residents and staff, low suicide rates could be expected. Only few studies have investigated
272 this, and with ambiguous results [23,24]. Finally, a depletion of individuals susceptible to suicide may
273 explain that the increased risk related to disease burden vanished with age. Irrespective of the
274 underlying reason, however, it is puzzling that the same pattern does not seem to emerge in individuals
275 with suicide attempt.

276 *Conclusion*

277 Co-existing psychiatric and somatic comorbidities is common in individuals with suicidal behavior.
278 Higher combined burden of psychiatric and somatic comorbidities increased the odds of suicidal
279 behavior, though the presence of somatic diseases had a potential protective effect on the risk of

280 suicide in older individuals. These findings support that both co-existence and burden of somatic and
281 psychiatric comorbidities are important components in suicide risk assessment and warrants
282 collaboration and enhanced awareness of suicidal behavior risks across somatic and psychiatric
283 departments.

284 **Acknowledgement statement**

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287 None.

288 **Conflicts of Interest statement**

289 The authors declare no conflicts of interest.

290 **Data availability statement**

291 According to Danish law, individual-level data cannot be shared by the authors.

292 **Supplementary Material**

293 For supplementary material accompanying this paper, visit [Cambridge.org/EPA](https://www.cambridge.org/EPA).

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357

358 **Figures**

359 **Figure 1.** Network graph depicting the 10 most common psychiatric vs. somatic diseases (using 10-
360 years of look back) and their internal relationship for A) individuals who died by suicide, B) individuals
361 who had a first-ever suicide attempt. Only prespecified psychiatric disorders and somatic diseases were
362 included in this analysis. In the network graph the proportion of individuals with a given disease is
363 illustrated by the size of the nodes whereas the co-existence of diseases is illustrated by the thickness of
364 the link drawn between the nodes. To avoid over-cluttering of the chord diagram, only diseases co-
365 occurring in more than xx% of individuals were visually linked to each other. Selection of psychiatric
366 disorders and somatic diseases was based on a data driven exploration of the data set performed for
367 each definition of outcomes, separately. As such, included diseases varied across outcomes.

368

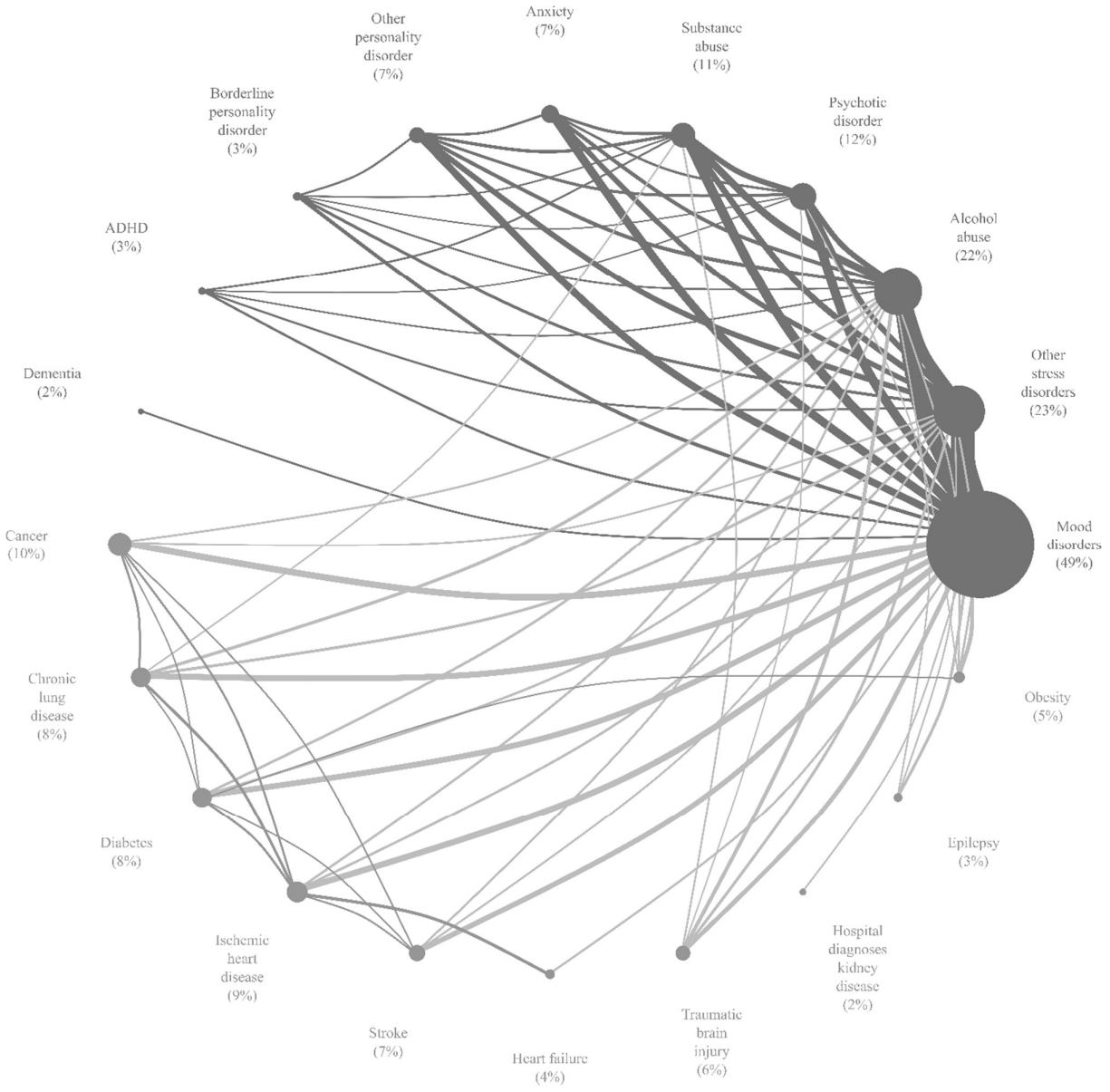
369

370 **Figure 2.** Heat map illustrating the probability of suicidal behavior depending on the burden of
371 psychiatric disorders and somatic diseases in combination i.e., the crude relative odds of experiencing
372 the outcome if having a specific combination of counts of somatic diseases vs. psychiatric disorders
373 using as reference the crude relative odds of experiencing the outcome if having 0 somatic diseases and
374 0 psychiatric disorders. A) individuals who died by suicide, B) individuals who had a first-ever suicide
375 attempt.

376 The number of psychiatric and somatic comorbidities is the total count of prespecified psychiatric vs.
377 somatic comorbidities listed under “psychiatric comorbidities” and “somatic comorbidities” in e-Table
378 1. In each cell of the grid, crude odds ratios (OR) and prevalence proportion is reported. The cells are
379 colored according to log (OR). OR is calculated using conditional logistic regression.

380

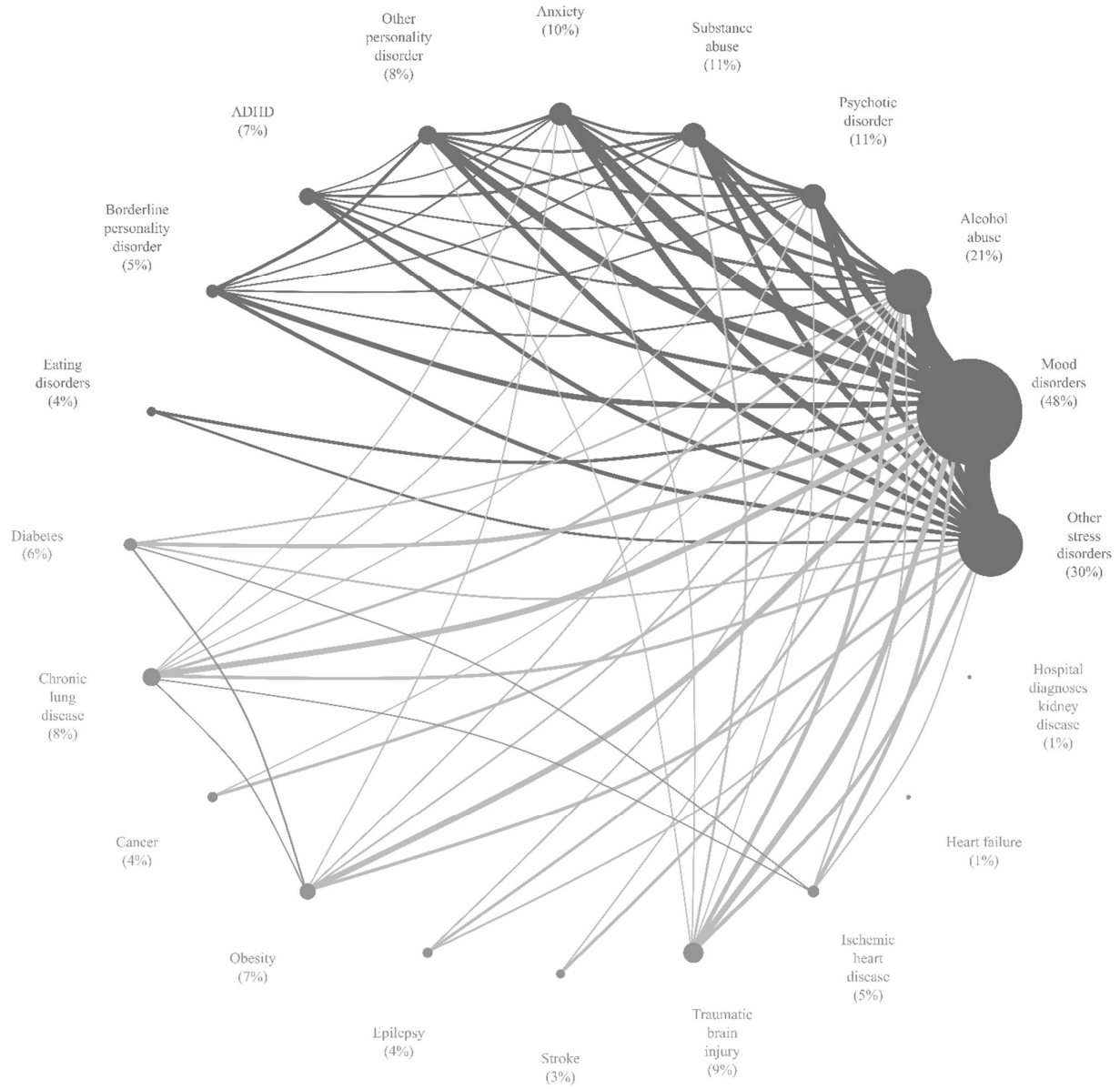
381 Figure 1a



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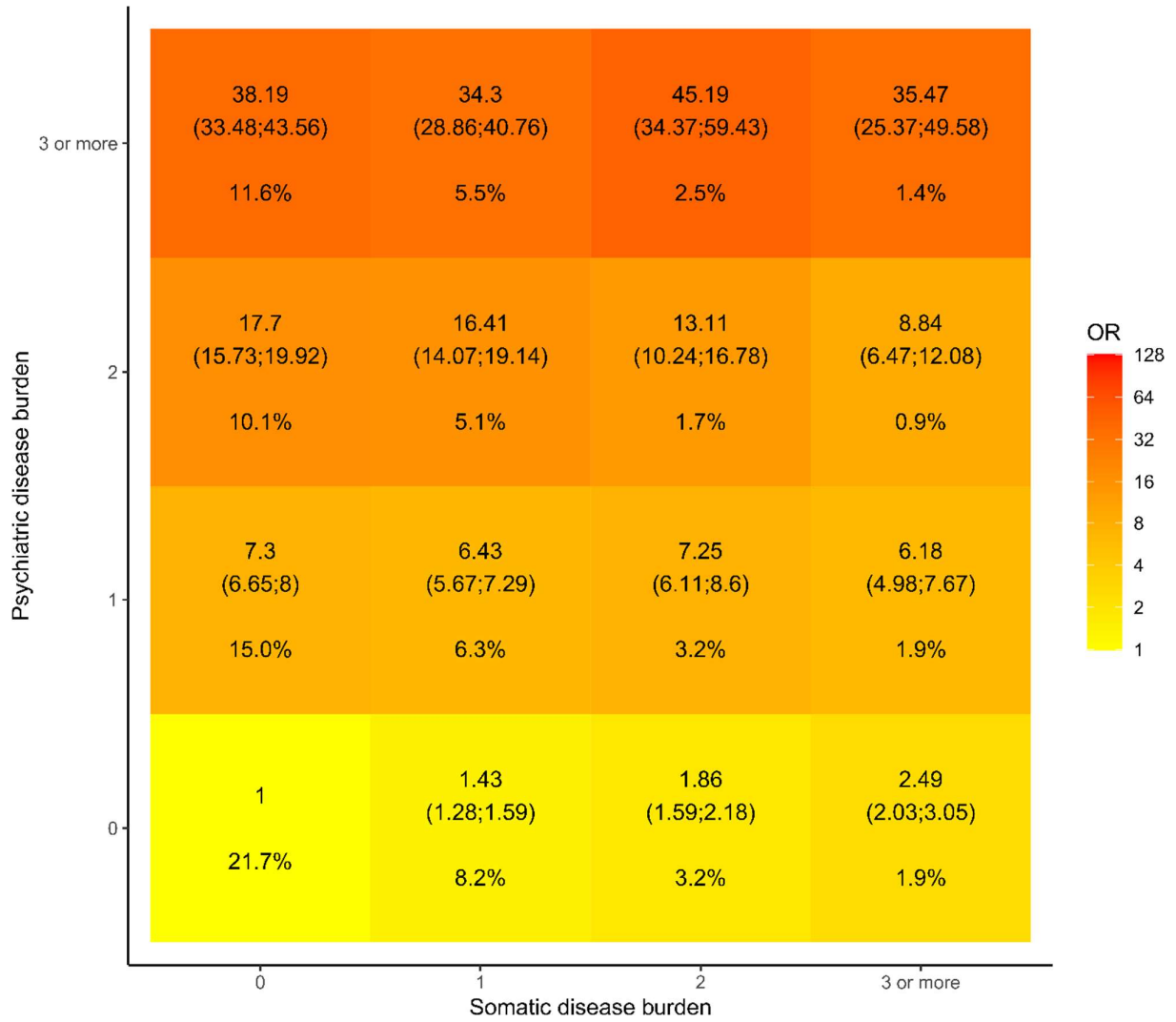
384 Figure 1b



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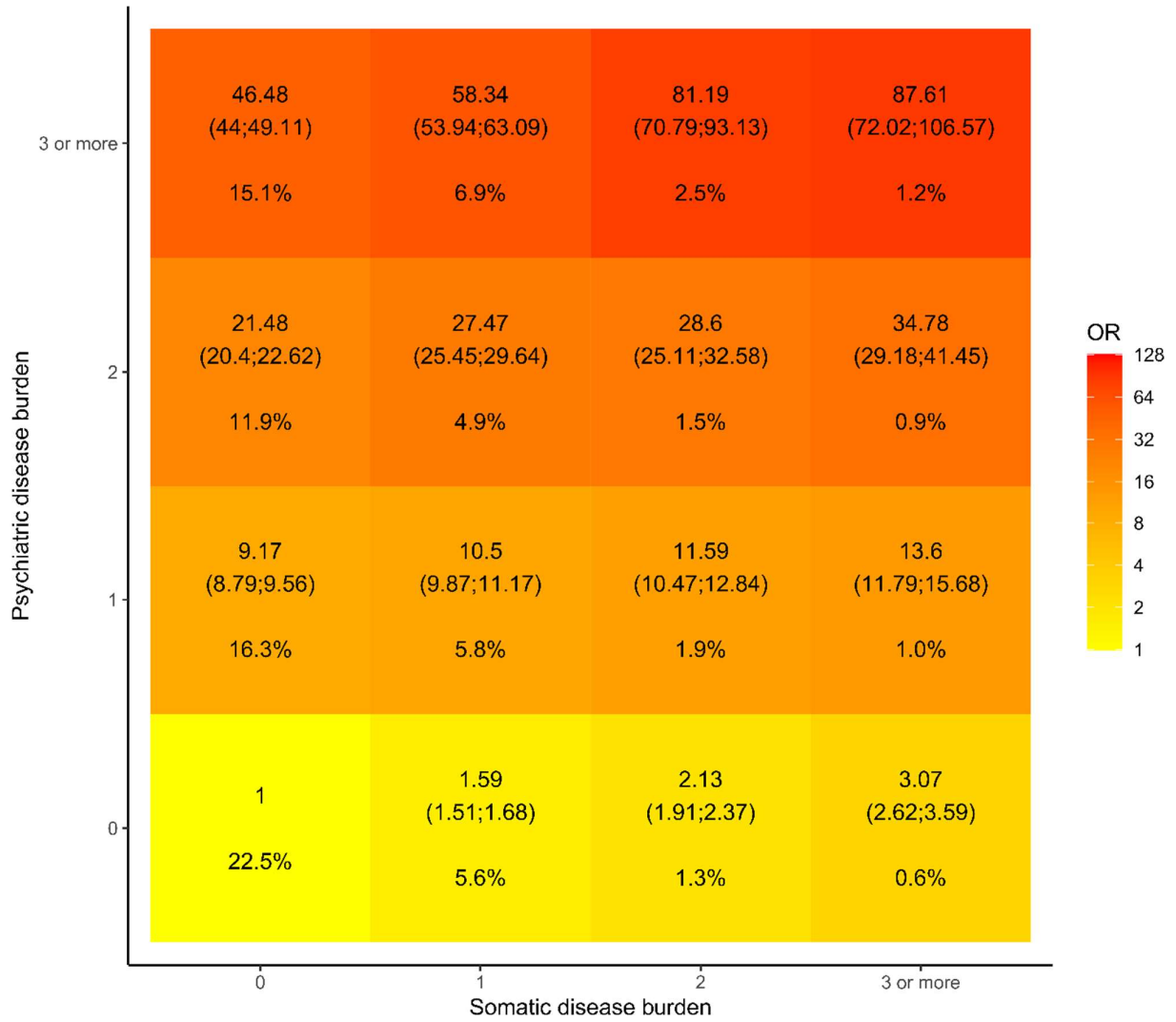
387 Figure 2a



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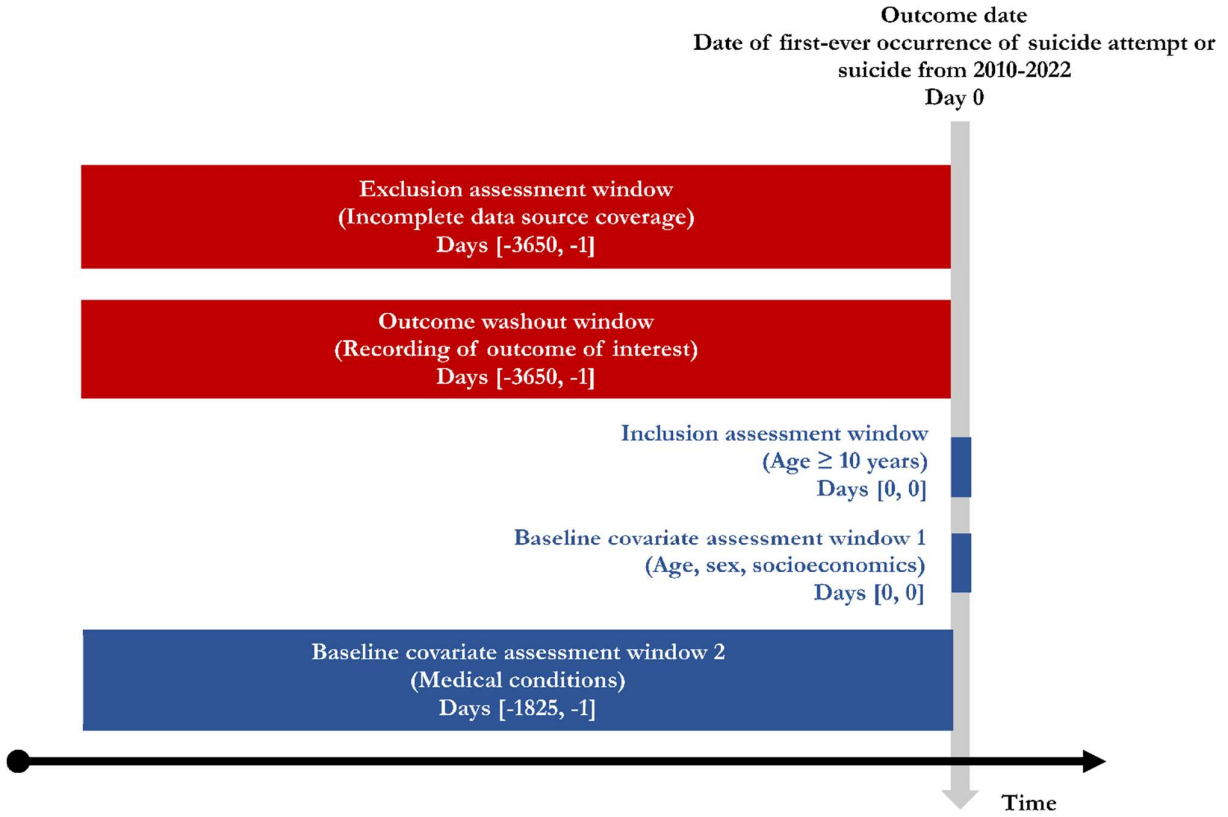
390 Figure 2b



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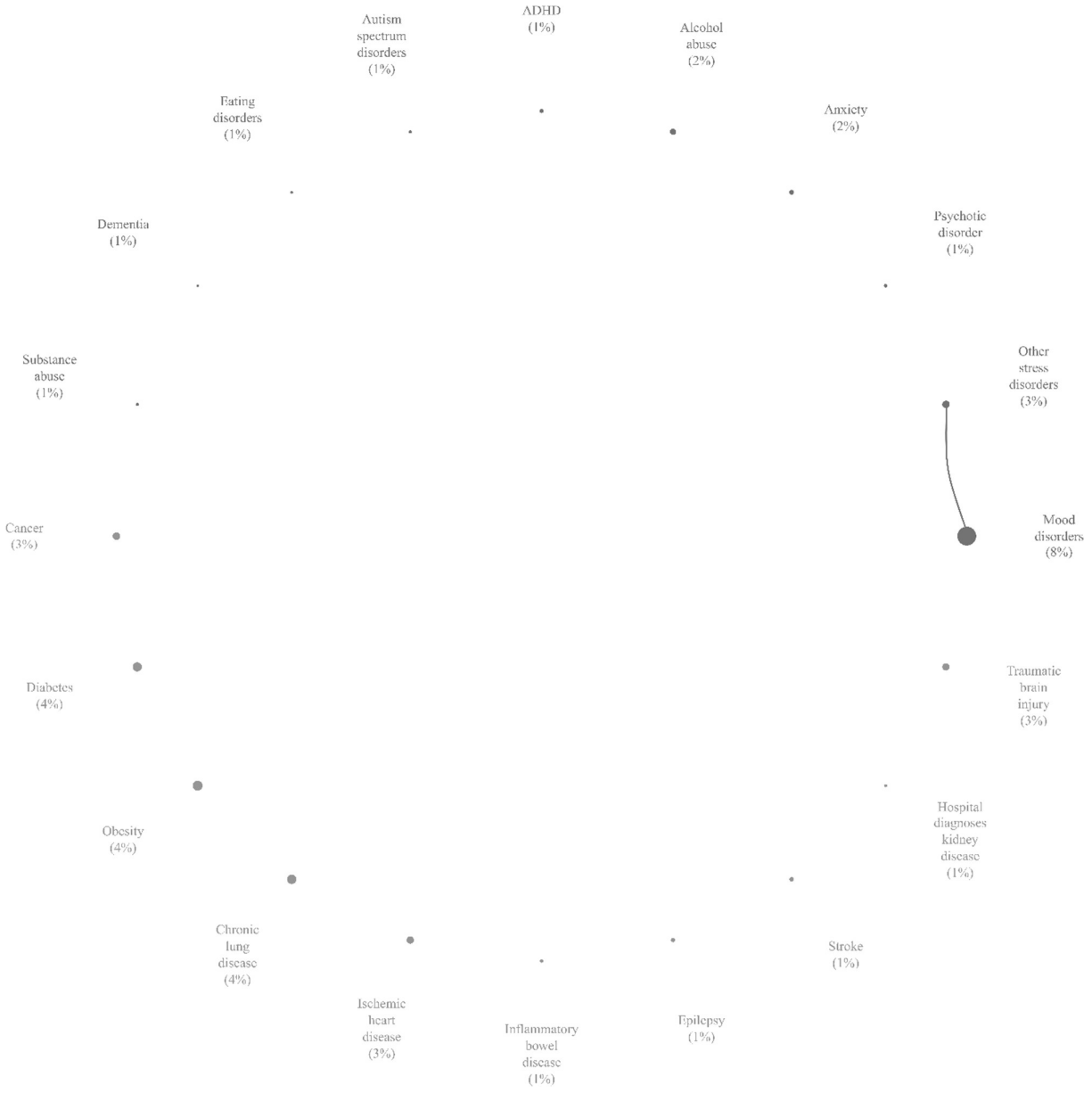
393 eFigure 1a



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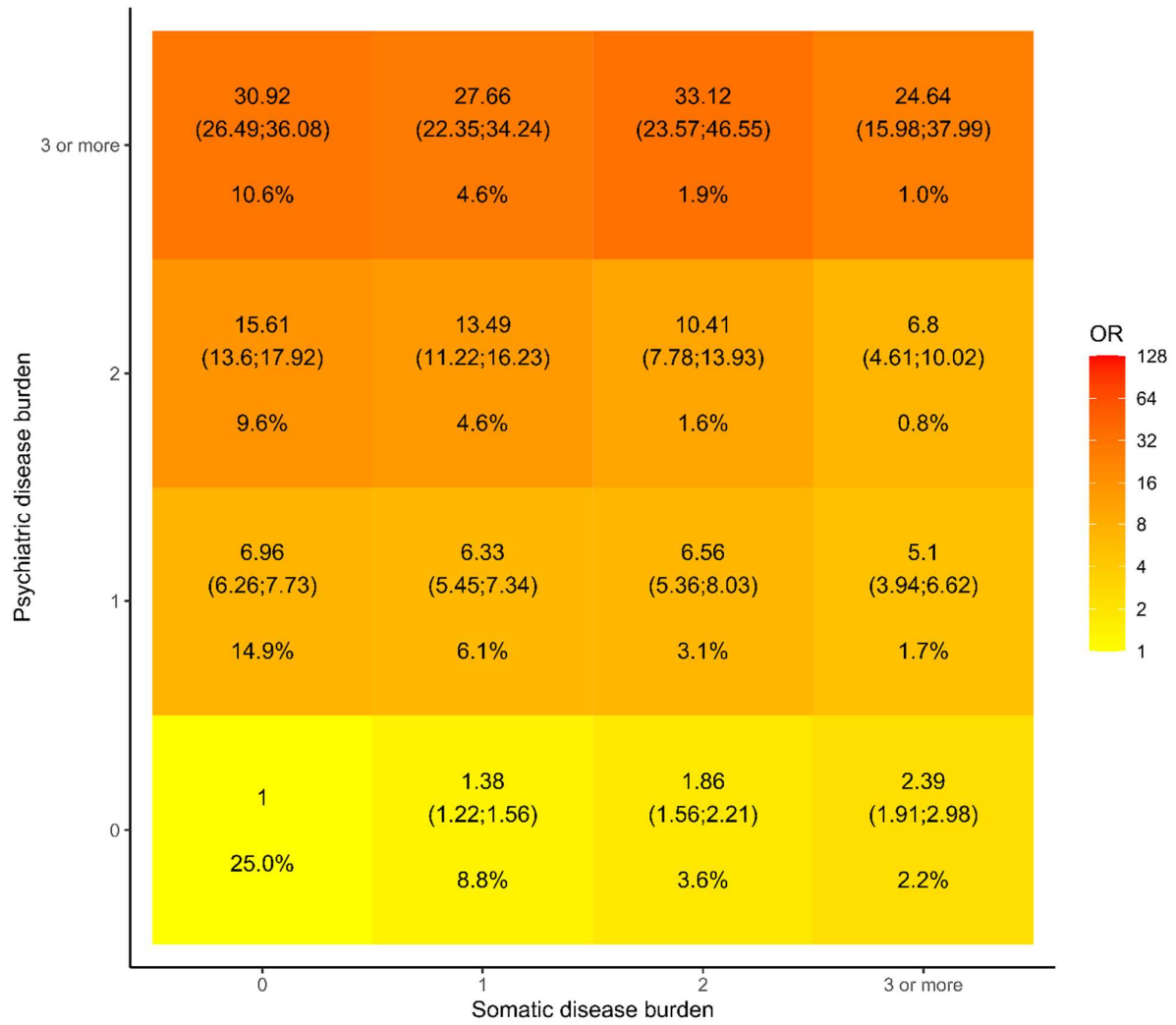
399 eFigure 2b



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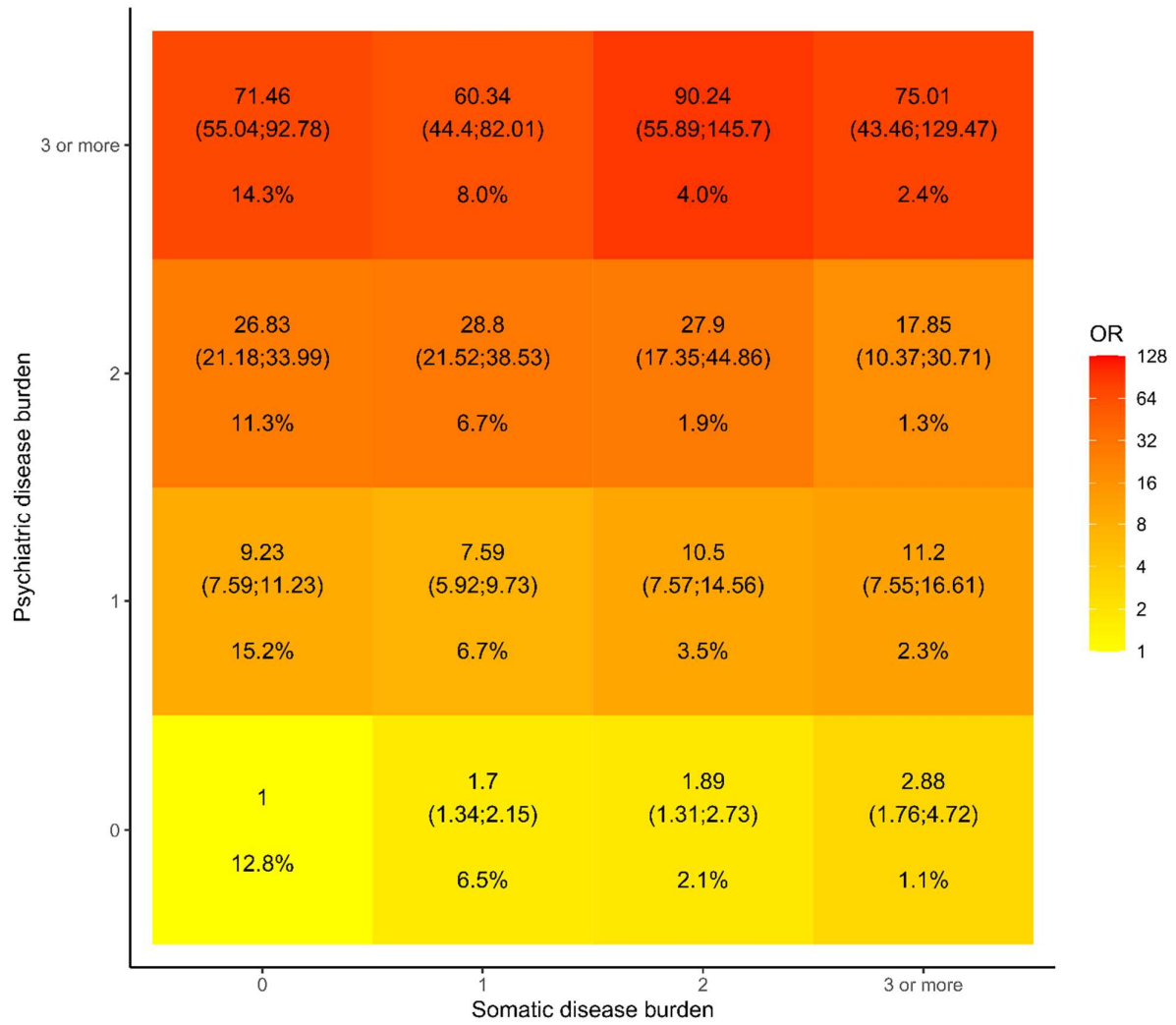
402 eFigure 3a



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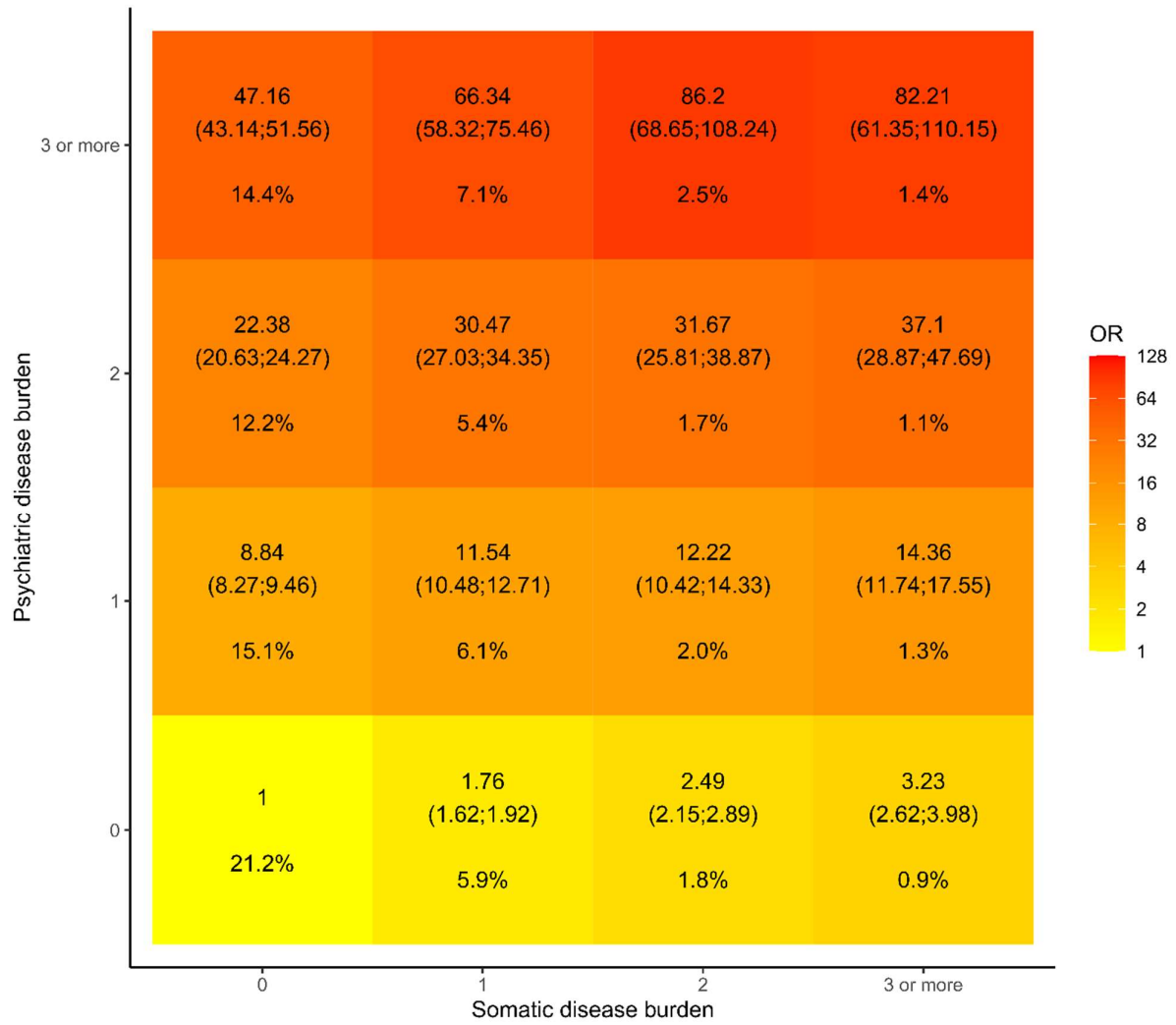
405 eFigure 3b



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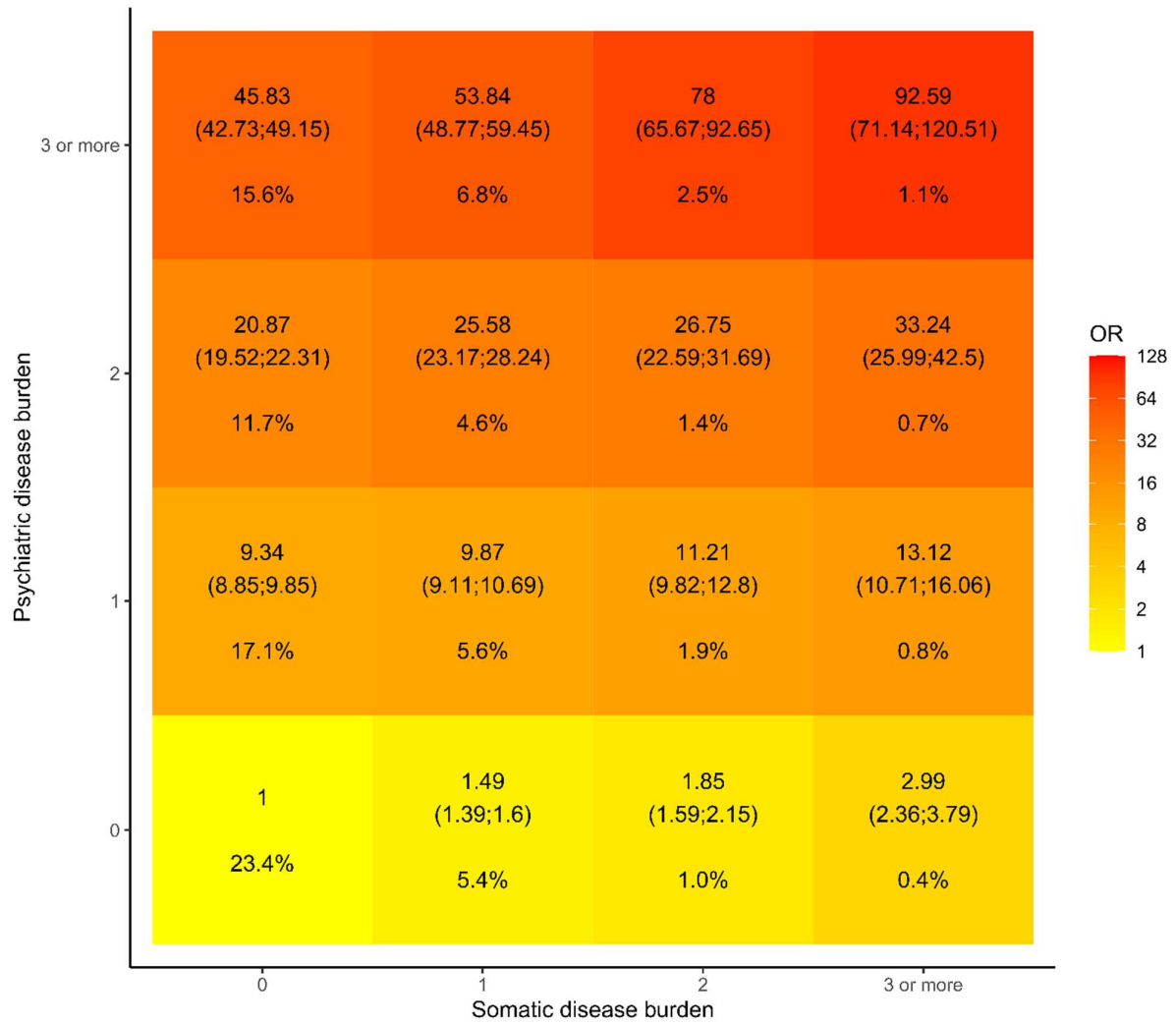
408 eFigure 3c



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411 eFigure 3d



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