Representativeness of survey participants in relation to mental disorders: a linkage between national registers and a population-representative survey

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Abstract

Introduction
Surveys and registers have provided important insights into the mental health of the community. However, both sources have strengths and limitations. While participation in surveys has been shown to be lower among those with mental disorders, misclassification and limited information on confounders are typical issues for registers.

Objectives
To examine if participants of the Central Denmark Region’s 2017 How are you? survey were representative of the general population in terms of mental disorder diagnoses.

Methods
By linking data from the Central Denmark Region’s 2017 How are you? survey with the Danish national registers, we compared the frequency of mental disorder diagnoses among (a) participants in the survey (n = 32,417), before and after applying non-response weights, and (b) the entire population who were eligible to participate (n = 1,063,082; 16 years of age or older on 10th January 2017 and registered as living in the Central Denmark Region). Using logistic regression models, we estimated associations between being diagnosed with any mental disorder and nine general medical conditions to assess whether selection into the survey appeared to bias these associations.

Results
Based on register data, 10.4% (n = 110,492) of the eligible population had received a diagnosis of any mental disorder prior to the date of this survey. Among the unweighted survey sample, 8.2% (n = 2,648) had received a diagnosis; once non-response weights were applied, this corresponded to 9.5%. Representativeness varied by sex, age and type of mental disorder. For example, people with organic disorders or substance use disorders were generally underrepresented among survey participants of all ages; however, representativeness of common disorders such as mood or neurotic disorders was generally good. With respect to the association of any mental disorder and general medical conditions, we found that estimates were similar for survey samples (both weighted and unweighted) compared to the entire eligible population.

Conclusions
People with a previous diagnosis of a mental disorder are slightly underrepresented in the survey. However, this selection bias was minimized when non-response weights were applied. Associations between mental disorders and general medical conditions did not appear to be affected by selection bias. With the application of non-response weights, the survey provided a sample representative of the general population in terms of mental disorder diagnoses.

Keywords
mental disorders; register-based research; survey-based research; epidemiology

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Introduction

Epidemiology is a foundational science for health research. In particular, it is essential to understand the prevalence of disorders, in order to design appropriate services [1]. Within the epidemiological tool box, surveys and register-based research have provided essential information to guide health planning. On one hand, surveys have played a critical role in mental health research. They can estimate the prevalence of different types of mental disorders, and explore service use and unmet need [2–4]. Whether these studies are multinational (e.g. World Mental Health Surveys [5] and the Wellcome Global Monitor [6]) or single site and smaller, population-based surveys have provided information on the epidemiology of mental health issues. On the other hand, several nations now have access to administrative registers (e.g. the Nordic countries) [7], which are useful to complement survey data. National registers, like electronic healthcare databases, provide large samples which often include the entire population, and thus are not subject to selection bias. However, the registers are administrative and often lack details about relevant exposures or confounders.

Each of these data sources have strengths and limitations. In particular, there are well known factors that influence participation in surveys [8–14]. Disorders associated with premature mortality may be underrepresented in surveys and previous research has also indicated that participation is lower in health surveys among people with poor mental health [15–17]. If selection into the survey is systematically different between those with and without disorders of interest, observed associations could be biased. This could be relevant, for example, in studies that use survey data to look at the associations between mental disorders and general medical conditions. Conversely, identifying cases based only on registers reflect those who seek help and not all health care provided may be included in register-based research [18]. This may mean surveys are a better source of information for mild mental disorders. Additionally, surveys and registers capture different details: while registers identify those who have received a diagnosis from a healthcare provider, surveys can provide greater depth by measuring symptoms and indicators of impairment [19–21]. Furthermore, the standardization of self-reported measures can be more culturally sensitive for measuring mental disorders [22]. Combining register data with survey data can fill these gaps [23, 24]. Register data can be supplemented by data from surveys on topics that registers do not capture well (e.g. work patterns [25], social relations [26], over-the-counter medication use [27], smoking [28], or alcohol intake) [28], while the registers can provide long follow-up periods or relevant confounders like education, income, health care utilization, comorbid diagnoses etc. Conversely, we can use the national registers to explore factors that influence selection bias in surveys. For example, survey participants can be compared to the general population to assess how representative participants are [29, 30].

When using a data source to find out information about a population, it is important to try to identify the data source’s limitations and, if possible, quantify them. In this article, we attempt to do this with a Danish population-based survey: How are you? (original Danish title Hvordan har du det?). It is also referred to as the Danish National Health Survey [31] and can be used to supplement the register data [31]. This survey has been run in 2010, 2014, 2017 and 2021. It is a national survey based on five regional stratified random samples and one national random sample, and is concerned with health-related quality of life, health behaviour, morbidity, and social relations in the Danish population. Weighting procedures are used in the survey to correct for survey design and non-response in relation to socio-demographic characteristics, visits to general practitioners, and somatic hospital admissions [31]; these weights ensure that participants are representative of the entire population regarding these characteristics. However, it is unknown the extent to which participants are representative regarding mental disorders. Several previous surveys have suggested that non-participants have more mental disorders than participants [9–12, 32, 33]. As data from How are you? is being used by researchers to describe health in Denmark, we believe it would be useful to consider how representative the survey population is. In this article, we aim to assess the extent of any selection bias with regards to mental disorder diagnoses in the 2017 Central Denmark Region How are you? survey, by comparing the frequency of diagnoses among survey participants, with the entire population eligible to participate in the survey. We make these comparisons by sex, age and type of mental disorder. Additionally, we estimate the association between mental disorders and general medical conditions in survey participants and in the eligible population. It is important to note that the Danish national registers are not free of limitations (as has been previously highlighted) [34, 35], however we hope that triangulation can help us to understand whether those with mental disorder diagnoses are well represented in the survey.

Methods

The Danish national registers

The Danish Civil Registration System holds continuously updated information on all individuals residing in Denmark [36]. Each person in the entire population is assigned a unique Central Person Register number, which allows linkage to person-level data in the other Danish national registers, including the health registers - for example, the National Patient Register [37, 38], which contains information on diagnoses made during hospital visits, or the Danish Psychiatric Central Research Register [39], which contains psychiatric diagnoses made during inpatient, outpatient and emergency visits. An introduction to the Danish national registers is provided by Thygesen and Ersboll [40].

The 2017 central Denmark region How are you? survey

The 2017 Central Denmark Region How are you? survey is a questionnaire-based survey, one of six mutually exclusive random subsamples that cover all of Denmark: one in each of the five Danish administrative regions, and one national sample [31, 41]. It is based on stratified random selection of participants who were 16 years of age or older on 10th January 2017 and were registered as living within the Central Denmark Region on that date, identified from the Danish
Civil Registration System (which includes the entire Danish population). The survey includes questions about participants’ health, including physical health, mental health and health behaviours (such as physical activity, smoking and alcohol intake) [31, 42, 43]. Survey data, such as that from this survey, can also be provided to Statistics Denmark to anonymize the data and link it to the national registers.

Approvals
The study was approved by the Danish Data Protection Agency, and data access was agreed by Statistics Denmark and the Danish Health Data Authority. According to Danish law, informed consent is not required for register-based studies. All data were de-identified and not recognizable at an individual level. The survey was reported to the Register of Research Projects of the Central Denmark Region (record number 1 16 02 593 16). All survey participants were informed that their survey data would be linked to the registers. Linkage was carried out by Statistics Denmark.

Study population and design
This cross-sectional study included the 1,063,082 individuals in Denmark who met the eligibility criteria for participating in the 2017 Central Denmark Region How are you? survey. A total of 52,000 persons were invited to participate in the survey. Invitation to participate was random in terms of all factors (e.g. sex, age, education), but stratification ensured coverage of all municipalities in the region (i.e. municipalities with fewer inhabitants were oversampled). The survey was sent out via secure Digital Post (a system used by Danish authorities and businesses to communicate with the population) or by regular postal services to the 10% of the invitees not registered to use digital post. The subsample not registered to use digital post received a paper questionnaire; these were mostly the elderly [31]. Those who did not respond after a reminder were sent a paper questionnaire and two reminders delivered to their home address. Invitees were informed that participation was voluntary and responses would be kept confidential. They were provided with contact details in case they had further questions and informed that participants would be entered into a prize draw. The response rate of 62% resulted in 32,417 participants. Those invited to participate were a random sample of the entire eligible population; however, it is unclear whether those who agreed to participate were representative of the eligible population. Statistics Denmark had access to information on both participants and non-participants, and they calculated non-response weights to correct for differences in selection probabilities (based on municipality) and response rates. These were constructed using a model-based calibration approach [44] based on information from the national registers on participants and non-participants (i.e., sex, age, municipality of residence, social background, and healthcare utilization through visits to general practitioners and somatic hospitals). These weights are made available with the survey data for use in statistical analyses. Once they are applied, the sample is expected to be representative of the target population at least in relation to the characteristics included in the model; however, these weights did not include direct information on mental disorders.

In this study, we explored the representativeness of the How are you? survey participants through several data obtained from national registers: demographic characteristics, proportion of participants who had been diagnosed with mental disorders before the survey was carried out, and associations between mental disorders and general medical conditions. Given that details of those who were invited to participate but declined cannot be provided for ethical reasons (thus, we could not identify non-responders in the registers), we carried out a comparison of survey participants with the entire eligible population.

A summary of the data obtained from each data source is provided in Supplementary Table 1. As mentioned above, all individuals who met the eligibility criteria to participate in the survey were identified in the Civil Registration System [36]. From here, we obtained details about each individual’s date of birth and sex. We linked them to their health and education data in other registers. Information on mental disorder diagnoses prior to the survey date was obtained from the Danish Psychiatric Central Research Register [39], which contains psychiatric diagnoses made in psychiatric inpatient contacts since 1969, and also in outpatient or emergency contacts since 1995, with a range of health care providers. Prior to 1994, diagnoses were coded according to International Classification of Diseases, version 8 (ICD-8); from 1994 onwards, ICD-10 was used. Mental disorders were ascertained in the period 1969 to January 2017. Details of the specific diagnoses and earliest age of diagnosis within each mental disorder group are presented in Supplementary Table 2 [45].

Information on nine categories of general medical conditions (circulatory, endocrine, pulmonary, gastrointestinal, urogenital, musculoskeletal, hematological, cancer and neurological; defined as in previous studies) [46, 47] was obtained. This was retrieved using the National Patient Register [37, 38] (which comprises data on diagnoses made during inpatient contacts since 1977, and also in outpatient or emergency contacts since 1995) and the Danish National Prescription Register [48] (which includes information on all redeemed prescriptions since 1995). General medical conditions were ascertained after individuals reached 1 year of age, from 1995 onwards, when prescription data became available. Criteria for the general medical conditions are presented in Supplementary Table 3.

Finally, information about the education group (primary/early childhood, secondary, above secondary, missing) in the year prior to the survey was obtained for each individual. This came from Statistics Denmark’s registers on education [49]. Information through responses from the How are you? survey was not used in this study, as those were only available for survey participants.

Statistical analysis
Statistical analyses were carried out in Stata 16 and Microsoft Excel. For all analyses, we considered three populations: the entire population eligible for the survey, survey participants, and survey participants after adjusting for non-response weights provided by Statistics Denmark. We ascertained the number of people within the categories of each of the following variables as of 10 January 2017: sex (male, female), age group.
### Results

The characteristics of the entire eligible population (1,063,082 individuals in Denmark who met the eligibility criteria for participating in the 2017 Central Denmark Region *How are you?* survey) and 32,417 survey participants before and after weights were applied are shown in Table 1.

Compared to the entire eligible population, there was underrepresentation of the following groups in the survey participants: males, individuals <45 years of age, and individuals with education up to primary/early childhood levels or missing education data. However, once the sampling weights were applied, characteristics of participants were more similar in terms of sex and age group.

Based on register data, 10.4% (n = 110,492) of the eligible population had received a diagnosis of any mental disorder prior to the date of the survey (see Supplementary Table 4). Among the unweighted survey sample, 8.2% (n = 2,648) had received a diagnosis; once weights were applied, this corresponded to 9.5%. Figure 1 shows the proportions in the entire eligible population, unweighted survey sample and weighted survey sample who had been diagnosed with any mental disorder and 10 specific types of mental disorders. While those with most types of mental disorders were, at least slightly, underrepresented, the largest relative differences were for organic disorders (prevalence of 0.57% in the eligible population and 0.30% in the weighted survey participants) and substance use disorders (prevalence of 1.87% in the eligible population and 1.37% in the weighted survey participants). For eating disorders (prevalence of 0.46% in the eligible

### Table 1: Characteristics of all those eligible for the 2017 Central Denmark Region How are you? survey and the survey participants (unweighted and weighted according to sampling and participation weights)

| Characteristic | Entire eligible population (n = 1,063,082) | Survey participants (n = 32,417) |
|---------------|------------------------------------------|----------------------------------|
|               | Unweighted | Weighted | P value from Chi squared test<sup>a</sup> | Unweighted | Weighted | P value from Chi squared test<sup>a</sup> |
| Sex           |            |          |                                     |            |          |                                     |
| Male          | 529,675    | 49.82 (49.73–49.92) | 15,105 | 46.60 (46.06–47.14) | <0.001 | 16,153 | 49.83 (49.18–50.47) | 0.973 |
| Female        | 533,407    | 50.18 (50.08–50.27) | 17,312 | 53.40 (52.86–53.94) | <0.001 | 16,264 | 50.17 (49.53–50.83) |
| Age group     |            |          |                                     |            |          |                                     |
| 16–24         | 162,736    | 15.31 (15.24–15.38) | 3,791 | 11.69 (11.35–12.04) | <0.001 | 4,962 | 15.31 (14.80–15.82) | 0.861 |
| 25–34         | 158,201    | 14.88 (14.81–14.95) | 3,424 | 10.56 (10.23–10.89) | <0.001 | 4,831 | 14.90 (14.39–15.42) |
| 35–44         | 163,108    | 15.34 (15.27–15.41) | 4,620 | 14.25 (13.88–14.64) | <0.001 | 4,979 | 15.36 (14.89–15.84) |
| 45–54         | 179,893    | 16.92 (16.85–17.00) | 5,915 | 18.25 (17.83–18.67) | <0.001 | 5,477 | 16.89 (16.43–17.36) |
| 55–64         | 159,126    | 14.97 (14.90–15.04) | 5,841 | 18.02 (17.60–18.44) | <0.001 | 4,843 | 14.94 (14.52–15.37) |
| 65–74         | 142,027    | 13.36 (13.30–13.42) | 5,703 | 17.59 (17.18–18.01) | <0.001 | 4,402 | 13.58 (13.19–13.97) |
| 75+           | 97,991     | 9.22 (9.16–9.27) | 3,123 | 9.63 (9.32–9.96) | <0.001 | 2,925 | 9.02 (8.68–9.38) |

<sup>a</sup>Comparing the frequencies observed in the unweighted and weighted survey participants, with the frequencies expected if the proportions had been the same as in the entire eligible population.

(16–24, 25–34, 35–44, 45–54, 55–64, 65–74, 75+ years), and education group (primary/early childhood, secondary, above secondary, missing). Additionally, we determined the number of people who had received a diagnosis of any mental disorder (ICD-10 F codes) and 10 specific types of mental disorders (each F code subgroup, as per Supplementary Table 2). We carried out Chi-squared tests to compare the frequencies of mental disorders observed in the survey sample, with the frequencies expected if the proportions had been the same as in the entire eligible population. For the observed frequencies, we calculated the frequencies as observed (i.e. unweighted, not taking the non-response weights into consideration), as well as the frequencies with the non-response weights (i.e. weighting each individual as per their assigned non-response weight to make the sample representative).

We then carried out the same descriptive analyses to consider the frequency of any mental disorder in each population disaggregated into fourteen groups depending on sex and age group. When looking at specific types of mental disorders in each population by sex and age, however, due to small numbers, we used broader age categories (16–34, 35–54, 55+ years), resulting in six groups.

Finally, we estimated associations between being diagnosed with any mental disorder and the nine general medical conditions (Supplementary Table 3) [46] through logistic regression models to calculate odd ratios (ORs) and 95% confidence intervals (CIs). These were estimated for the three populations to assess whether the associations were different in survey participants. The models were adjusted for sex, age group and education.
Figure 1: Prevalence of mental disorder diagnoses between all those eligible for the 2017 Central Denmark Region How are you? survey and the survey participants (before and after weights were applied).

The results for types of mental disorders by sex and age group are shown in Supplementary Figure 1 and Supplementary Table 6. Again, there was variation in representation of types of mental disorders by sex and age group. For example, people with organic disorders or substance use disorders were underrepresented among survey participants; however, representativeness of common disorders such as mood, neurotic, and behavioral disorders was generally good, especially for females.

Logistic regression models were used to explore the odds of general medical condition comorbidity among those with any mental disorder diagnosis, compared to those without a mental disorder diagnosis, in each of the three populations separately. For example, in all three populations, those with a
mental disorder were at increased odds of a circulatory medical condition; although the point estimates differed slightly for each population, the conclusion would be similar. This was the case for most general medical conditions: the ORs were similar for the survey samples (both weighted and unweighted) compared to the entire eligible population (Figure 3 and Supplementary Table 7), suggesting that associations among survey participants were not biased. However, for some general medical conditions, differences were observed e.g. the OR for the entire eligible population was lower than the ORs for the survey samples for endocrine conditions and pulmonary conditions.

Discussion

By combining the Danish register data with data from the 2017 Central Denmark Region How are you? survey, we have shown that people with a previous diagnosis of a mental disorder are underrepresented in the survey. However, this selection problem is minimized when sampling weights are applied. This pattern is not the same across all age groups, or even all mental disorders, with underrepresentation not observed for eating disorders or developmental disorders, and minimal for others (e.g. personality disorders or behavioral disorders). Additionally, while selection may be an issue for some sex- and age- groups for some mental disorder types, associations between mental disorders and general medical conditions do not appear to be strongly affected by selection bias.

The application of non-response weights meant that the survey provided a sample representative of the entire eligible population in terms of a range of characteristics, including sex and age group. While the survey underrepresents those with mental disorder diagnoses, we found that this bias was relatively small. People diagnosed with any mental disorder represented 10.4% of the entire eligible population; among the weighted survey participants, this was less than 1%-point less (9.5%). The weighted survey participants were also fairly representative in terms of specific types of mental disorders: for the most common types of disorders, neurotic disorders, 5.1% of the entire eligible population had received a diagnosis, compared to 4.7% of the weighted survey participants. The slight overrepresentation of those with eating disorders may reflect characteristics observed in individuals with eating disorders [50]. This variation should be considered by researchers when carrying out surveys that are used to investigate mental health. The response rates to surveys
Figure 3: Odds ratios (and 95% confidence intervals) for associations between any mental disorder and nine general medical conditions, among all those eligible for the 2017 Central Denmark Region *How are you?* survey and the survey participants (before and after weights were applied)

| General Medical Condition | Crude models | Adjusted models |
|---------------------------|--------------|-----------------|
| Circulatory system        |              |                 |
| Endocrine system          |              |                 |
| Pulmonary system          |              |                 |
| Gastrointestinal system   |              |                 |
| Urogenital system         |              |                 |
| Musculoskeletal system    |              |                 |
| Hematological system      |              |                 |
| Cancers                   |              |                 |

Adjusted models included sex, age group, and education.

have been generally declining [51, 52], which can affect their generalizability and the representativeness compared to the target populations [53]. However, the *How are you?* surveys have maintained reasonable response rates, with the 2017 Central Denmark Region survey achieving 62%. Bias may be more impactful in surveys that have low response rates, but applying weights may mitigate this [54]. A recent study considering primary health care utilization in Danish registers and the same survey highlights the importance of applying the calibrated survey weights to address non-response; it concluded that applying the weights reduced the bias caused by differential selection [55].
The observation that people with mental disorder diagnoses are slightly underrepresented in the HHDD survey is in line with descriptions of other surveys. Two surveys in the Dutch population reported that depression and anxiety symptoms were more common in non-participants than participants [32, 33]. A study in the United States found that those with records of substance use were underrepresented [11]. A Finnish register based study reported that subjects (across sexes and education levels) with any psychiatric disorder, as identified in the Finnish Hospital Discharge Register, participated less in their survey than those without psychiatric disorders [9]. Haapea et al. [9] discuss this as possibly resulting due to characteristics associated with some mental disorders e.g. passivity or cognitive impairment, which may be supported by the underrepresentation of people with organic disorders in the Danish survey. Studies of individuals with schizophrenia suggested that longer duration [10] and increased severity [10, 12] of schizophrenia were less likely to participate. While some surveys have managed reasonable response rates among people with organic disorders [56, 57], Paganini-Hill et al. [57] reported that there appeared to be a higher proportion of dementia on death records among non-responders to their survey. For those with cognitive impairments (e.g. dementia, intellectual disabilities, etc), participation may not be possible. Therefore, the survey may not be representative of this group. If researchers want to try to increase participation among people with mental disorders, and in particular these subgroups, they may need to take further measures to target them. Stolzmann et al. [58] discuss that pen-and-paper surveys are generally better for conducting surveys among people with mental disorders, as information technology based-methods have varying levels of use and desirability among those with mental health conditions.

There are limitations of our study that should be considered when interpreting the results. First, the Danish national registers, which we compare the survey to, cannot be considered a ‘gold standard’ for identifying people with mental disorders. The Danish Psychiatric Central Research Register includes information on hospital contacts for mental disorders (inpatient, outpatient, and emergency room visits), but we do not have any information on mental disorders treated only in general practice or by independent psychiatrists and psychologists, or on people who do not seek any medical treatment for their mental disorders. As a result, it is likely that the national registers are more likely to identify more severe cases of mental disorders. Therefore, they may not be able to indicate representation of people with milder cases of mental disorders. Second, it is not possible to identify people who have recovered from mental disorders in the Danish Psychiatric Central Research Register. Our study classifies anyone who had received a mental disorder diagnosis prior to survey eligibility as having a mental disorder; however, it is possible that individuals will no longer have the mental disorder by the time they decided whether to respond to the survey. Therefore, misclassification is possible in both directions. However, it should be considered that by combining the surveys and the registers, we are trying to improve our understanding of the limitations of these data sources – research can, and should, continue to consider these, with the aim of providing estimates of mental disorder prevalence [23, 24]. Third, selection bias could also arise from excess mortality if a disorder is associated with increased risk of premature mortality. However, we defined our study population as being eligible to participate in the survey, and this selection mechanism would have affected both survey participants and the eligible population.

Our work could help guide other researchers with access to both survey and administrative data when considering and designing future studies aimed at measuring the representativeness of survey data. Combining data sources may provide opportunities to better understand our data [59]. This type of survey-register linkage could provide more precise non-response weights in relation to mental disorders, or could use quantitative bias analysis techniques to adjust for selection bias [60]. This investigation of survey data is a useful task to understand our data sources and there is a need to replicate this work in other surveys, and especially in child and youth samples. Additionally, there is a need to explore representativeness across other population indicators, for example other health conditions or immigrant status.

Although people with mental disorder diagnoses are underrepresented in the 2017 Central Denmark Region How are you? survey, this appears to be a relatively minor issue after sampling weights are applied. In other surveys, if researchers want to investigate the prevalence of mental disorders, they need to consider the possibility of underrepresentation, which may reduce a survey’s ability to indicate absolute numbers of mental disorders in a population of interest. However, when looking at the association between any mental disorders and general medical conditions, the results for survey participants (both weighted and unweighted) were similar results to those obtained for the entire eligible population – the 2017 Central Denmark Region How are you? survey appears to provide a good sample to do this type of research.

Declaration of interest
The authors have no declarations of interest.

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Ethics statement
The study was approved by the Danish Data Protection Agency. Access to individual-level Denmark data is governed
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### Supplementary Table 1: Summary of the data sources used

| Data source name                          | Data source type            | Description of the data source                                                                 | Description of the data used in this research article                                                                                                                                                                                                 |
|-------------------------------------------|-----------------------------|-----------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Danish Civil Registration System          | Danish national register    | Continuously updated information on all individuals residing in Denmark from 1968 onwards. Each individual is assigned a unique personal identification number, which links their data across all Danish registers. | All individuals eligible for participation were identified (i.e. 16 years of age or older on 10th January 2017 and were registered as living within the Central Denmark Region on that date).                                                                                                                                  |
| Danish Psychiatric Central Research Register | Danish national register    | Psychiatric diagnoses made in psychiatric inpatient contacts since 1969, and also in outpatient or emergency contacts since 1995, with a range of health care providers. Prior to 1994, diagnoses were coded according to International Classification of Diseases, version 8 (ICD-8); from 1994 onwards, ICD-10 was used. | Mental disorder diagnoses made between 1969 and January 2017 in all individuals eligible for participation (as identified in the Danish Civil Registration System).                                                                                                                               |
| Danish National Patient Register          | Danish national register    | Diagnoses made during inpatient contacts (since 1977), outpatient or emergency contacts (since 1995). Prior to 1994, diagnoses were coded according to ICD-8; from 1994 onwards, ICD-10 was used. | Relevant diagnoses were used (in conjunction with prescription data) to ascertain general medical conditions in individuals eligible for participation.                                                                                                                                                        |
| Danish National Prescription Register     | Danish national register    | Information on all redeemed prescriptions since 1995.                                        | Prescription data were used (in conjunction with diagnosis data from the Danish National Patient Register) to ascertain general medical conditions in individuals eligible for participation.                                                                                                                                 |
| Statistics Denmark’s registers on education | Danish national register    | Annual data since 1981 on the highest level of education attained.                              | Educational level in 2016, grouped into the following categories: primary/early childhood, secondary, above secondary, missing.                                                                                                                                                                                   |
| 2017 Central Denmark Region How are you? survey | Regional population based survey | Questionnaire-based survey on health, based on stratified random selection of 32,417 participants who were 16 years of age or older on 10th January 2017 and were registered as living within the Central Denmark Region on that date, identified from the Danish Civil Registration System. | Survey participants were compared to the eligible population (identified from the Danish Civil Registration System).                                                                                                                                                                                                 |
## Mental Disorders

### Examples of diagnoses included in each group

| Mental Disorders                                                                 | ICD-10       | ICD-8 equivalency                                                                 | Earliest age of diagnosis (years) |
|----------------------------------------------------------------------------------|--------------|-----------------------------------------------------------------------------------|----------------------------------|
| Organic, including symptomatic, mental disorders                                | F00–F09      | 290.09, 290.10, 290.11, 290.18, 290.19, 292.x9, 293.x9, 294.x9, 309.x9               | 35                               |
| Includes dementia in Alzheimer’s disease, vascular dementia, etc.               |              |                                                                                   |                                  |
| Mental and behavioral disorders due to psychoactive substance use                | F10–F19      | 291.x9, 294.39, 303.x9, 303.20, 303.28, 303.90, 304.x9                             | 10                               |
| Includes use of alcohol, cannabis, cocaine, nicotine, opioids, sedatives, hypnotics, anxiolytics, etc. |              |                                                                                   |                                  |
| Schizophrenia and related disorders                                             | F20–F29      | 295.x9, 296.89, 297.x9, 298.99, 299.04, 299.05, 301.83                           | 10                               |
| Includes schizophrenia, schizotypal disorders, schizoaffective disorders and other psychotic disorders. |              |                                                                                   |                                  |
| Mood disorders                                                                    | F30–F39      | 296.x9 (excluding 296.89), 298.09, 298.19, 300.49, 301.19                      | 10                               |
| Includes bipolar disorder, depressive disorders, etc.                           |              |                                                                                   |                                  |
| Neurotic, stress-related, and somatoform disorders                               | F40–F48      | 300.x9 (excluding 300.49), 305.x9, 305.68, 307.99                              | 5                                |
| Includes anxiety disorders, phobias, obsessive compulsive disorders, etc.        |              |                                                                                   |                                  |
| Eating disorders                                                                 | F50          | 306.50, 306.58, 306.59                                                           | 1                                |
| Includes anorexia nervosa, bulimia nervosa, etc.                                 |              |                                                                                   |                                  |
| Specific personality disorders                                                   | F60          | 301.x9 (excluding 301.19), 301.80, 301.81, 301.82, 301.84                      | 10                               |
| Intellectual Disabilities                                                        | F70–F79      | 311.xx, 312.xx, 313.xx, 314.xx, 315.xx                                           | 1                                |
| Pervasive developmental disorders                                               | F84          | 299.00, 299.01, 299.02, 299.03                                                   | 1                                |
| Includes autism spectrum disorders                                               |              |                                                                                   |                                  |
| Behavioral and emotional disorders with onset usually occurring in childhood and adolescence | F90–F98      | 306.x9, 308.0x                                                                  | 1                                |
| Includes attention-deficit hyperactivity disorder, conduct disorders, childhood emotional disorders, etc. |              |                                                                                   |                                  |
Supplementary Table 3: Definitions of the general medical conditions included in each category

| Category                          | Coding definition                                                                 | Diagnosis codes (ICD-10) | Drug codes (ATC)   | Time frame for prescriptions |
|----------------------------------|-----------------------------------------------------------------------------------|---------------------------|--------------------|------------------------------|
| **Circulatory system**           |                                                                                   |                           |                    |                              |
| Hypertension                     | Diagnosis AND/OR prescriptions of antihypertensives\(^a\)                        | I10–I13, I15              | C02, C03, C04, C07, C08, C09 | Twice in 1 year              |
| Dyslipidemia                     | Diagnosis AND/OR prescription of lipid-lowering drugs\(^b\)                      | E78                       | C10                | Twice in 1 year              |
| Ischemic heart disease           | Diagnosis AND/OR prescription for antianginal drug                               | I20–I25                   | C01DA              | Twice in 1 year              |
| Atrial fibrillation              | Diagnosis                                                                        | I48                       |                    |                              |
| Heart failure                    | Diagnosis                                                                        | I50                       |                    |                              |
| Peripheral artery occlusive      | Diagnosis                                                                        | I70–I74                   |                    |                              |
| Stroke                           | Diagnosis                                                                        | I60–I64, I69              |                    |                              |
| **Endocrine system**             |                                                                                   |                           |                    |                              |
| Diabetes mellitus                | Diagnosis AND/OR prescription of antidiabetics                                    | E10–E14                   | A10A, A10B         | Twice in 1 year              |
| Thyroid disorder                 | Diagnosis AND/OR prescription of thyroid therapy drugs                           | E00–E05, E061–E069, E07   | H03                | Twice in 1 year              |
| Gout                             | Diagnosis                                                                        | E79, M10                  |                    |                              |
| **Pulmonary system and allergy** |                                                                                   |                           |                    |                              |
| Chronic pulmonary disease        | Diagnosis AND/OR prescription for obstructive airway disease drugs               | J40–J47                   | R03                | Twice in 1 year              |
| Allergy                          | Diagnosis AND/OR prescription for non-sedative antihistamines AND/OR nasal antiallergics | J30.1–J30.4, L23, L50.0, T78.0, T78.2, T78.4 | R06AX, R06AE07, R06AE09, R01AC, R01AD | Twice in 1 year |
| **Gastrointestinal system**      |                                                                                   |                           |                    |                              |
| Ulcer/chronic gastritis          | Diagnosis                                                                        | K221, K25–K28, K293–K295 |                    |                              |
| Chronic liver disease            | Diagnosis                                                                        | B16–B19, K70, K74, K766, I85 |                    |                              |
| Inflammatory bowel disease       | Diagnosis                                                                        | K50–K51                  |                    |                              |
| Diverticular disease of intestine| Diagnosis                                                                        | K57                      |                    |                              |
| **Urogenital system**            |                                                                                   |                           |                    |                              |
| Chronic kidney disease           | Diagnosis                                                                        | N03, N11, N18–N19         | C02CA, G04C        | Twice in 1 year              |
| Prostate disorders               | Diagnosis AND/OR prescription of prostate hyperplasia therapy drugs               | N40                       |                    |                              |
| **Musculoskeletal System**       |                                                                                   |                           |                    |                              |
| Connective tissue disorders      | Diagnosis                                                                        | M05–M06, M08–M09, M30–M36, D86 | M05B, G03XC01, H05AA | Twice in 1 year              |
| Osteoporosis                     | Diagnosis AND/OR prescription for osteoporosis drugs                             | M80–M82                  | N02A, N02BA51, N02BE, M01A, M02A | 4x in 1 year |
| Painful conditions               | Repeated prescriptions of analgesics                                             |                           |                    |                              |
| **Hematological system**         |                                                                                   |                           |                    |                              |
| HIV/AIDS                         | Diagnosis                                                                        | B20–B24                  |                    |                              |
| Anemias                          | Diagnosis                                                                        | D50–D53, D55–D59, D60–D61, D63–D64 |                    |                              |
| Cancers                          | Diagnosis                                                                        | C00–C43, C45–C49         |                    |                              |
| **Neurological system**          |                                                                                   |                           |                    |                              |
| Vision problems                  | Diagnosis                                                                        | H40, H25, H54             |                    |                              |
| Hearing problems                 | Diagnosis                                                                        | H90–H91, H931            |                    |                              |
| Migraine                         | Diagnosis AND/OR prescription of specific anti-migraine drugs                    | G43                      | N02C               | Twice in 1 year              |
| Epilepsy                         | Diagnosis AND/OR prescription of anti-epileptics                                | G40–G41                  | N03                | Twice in 1 year              |
| Parkinson’s disease              | Diagnosis                                                                        | G20–G22                  |                    |                              |
| Multiple sclerosis               | Diagnosis                                                                        | G35                      |                    |                              |
| Neuropathies                     | Diagnosis                                                                        | G50–G64                  |                    |                              |

\(^a\) Ascertained only in absence of ischemic heart disease/heart failure, and by diuretics only if no kidney disease.

\(^b\) Prescriptions used if no previous ischemic heart disease.
## Supplementary Table 4: Frequency of mental disorder diagnoses in the eligible population in the Central Denmark Region and the How are you? survey participants (unweighted and weighted)

| Mental disorders                  | Entire eligible population (n = 1,063,082) | Survey participants (n = 32,417) | Unweighted | Weighted | P value from Chi squared test<sup>a</sup> | P value from Chi squared test<sup>a</sup> |
|-----------------------------------|------------------------------------------|---------------------------------|------------|----------|------------------------------------------|------------------------------------------|
| Any mental disorder              | 110,492 (10.39 (10.34–10.45))            | 2,648 (8.17 (7.88–8.47))        | <0.001     | 3,064    | 9.45 (9.06–9.85)                         | <0.001                                   |
| Organic disorders                | 6,096 (0.57 (0.56–0.59))                 | 78 (0.24 (0.19–0.30))           | <0.001     | 97 (0.30 (0.23–0.39))                    | <0.001                                   |
| Substance use disorders          | 19,862 (1.83 (1.84–1.89))                | 365 (1.13 (1.02–1.25))          | <0.001     | 4445 (1.37 (1.22–1.55))                  | <0.001                                   |
| Schizophrenia                    | 13,584 (1.28 (1.26–1.30))                | 257 (0.79 (0.70–0.90))          | <0.001     | 34350 (1.08 (0.94–1.24))                 | 0.001                                    |
| Mood disorders                   | 47,131 (4.43 (4.39–4.47))                | 1,179 (3.64 (3.33–3.85))        | <0.001     | 1,332    | 4.11 (3.85–4.38)                         | 0.005                                    |
| Neurotic disorders               | 53,778 (5.06 (5.02–5.10))                | 1,299 (4.01 (3.80–4.23))        | <0.001     | 1,517    | 4.68 (4.40–4.98)                         | 0.002                                    |
| Eating disorders                 | 4,937 (0.46 (0.45–0.48))                 | 132 (0.41 (0.34–0.48))          | 0.160      | 171      | 0.53 (0.44–0.64)                         | 0.076                                    |
| Personality disorders            | 19,970 (1.88 (1.85–1.90))                | 489 (1.51 (1.38–1.65))          | <0.001     | 571      | 1.76 (1.59–1.95)                         | 0.114                                    |
| Intellectual disabilities        | 4,226 (0.40 (0.39–0.41))                 | 71 (0.22 (0.17–0.28))           | <0.001     | 99       | 0.30 (0.23–0.40)                         | 0.007                                    |
| Developmental disorders          | 5,616 (0.53 (0.51–0.54))                 | 129 (0.40 (0.33–0.47))          | 0.001      | 174      | 0.54 (0.44–0.65)                         | 0.895                                    |
| Behavioral disorders             | 19,158 (1.80 (1.78–1.83))                | 411 (1.27 (1.15–1.40))          | <0.001     | 564      | 1.74 (1.56–1.94)                         | 0.403                                    |

<sup>a</sup>Comparing the frequencies observed in the unweighted and weighted survey participants, with the frequencies expected if the proportions had been the same as in the entire eligible population.

## Supplementary Table 5: Frequency of any mental disorder diagnosis in specific sex- and age-groups within of the eligible population in the Central Denmark Region and the How are you? survey participants (unweighted and weighted)

| Sex | Age (years) | Number in group | Frequency of any mental disorder diagnosis % (95% CI) | Sex | Age (years) | Number in group | Frequency of any mental disorder diagnosis % (95% CI) | Unweighted | Weighted | P value from Chi squared test<sup>a</sup> | P value from Chi squared test<sup>a</sup> |
|-----|-------------|-----------------|------------------------------------------------------|-----|-------------|-----------------|------------------------------------------------------|------------|----------|------------------------------------------|------------------------------------------|
| Females 16–24 | 79,352 | 9,424 | 11.88 (11.65–12.10) | Females 25–34 | 76,389 | 11,200 | 14.66 (14.41–14.91) | 0.001 | 368 | 15.78 (13.99–17.76) | 0.590 |
| 25–34 | 80,811 | 10,702 | 13.24 (13.01–13.48) | 35–44 | 88,988 | 9,889 | 11.12 (10.91–11.32) | 0.001 | 315 | 11.60 (10.32–13.08) | 0.913 |
| 35–44 | 82,297 | 7,833 | 9.83 (9.63–10.04) | 55–64 | 79,675 | 7,333 | 8.14 (7.94–8.34) | 0.001 | 237 | 8.76 (8.51–11.18) | 0.010 |
| 45–54 | 90,935 | 8,515 | 10.63 (10.37–10.88) | 65–74 | 71,964 | 5,856 | 6.45 (6.22–6.69) | 0.125 | 560 | 6.50 (6.22–6.79) | 0.007 |
| 55–64 | 79,451 | 6,752 | 8.50 (8.31–8.69) | 75+ | 56,258 | 5,976 | 10.63 (10.37–10.88) | 0.004 | 269 | 10.57 (9.06–12.29) | 0.002 |
| 65–74 | 70,063 | 4,577 | 6.53 (6.35–6.72) | 75+ | 41,733 | 2,691 | 6.45 (6.22–6.69) | 0.001 | 307 | 6.50 (6.22–6.79) | 0.007 |

<sup>a</sup>Comparing the frequencies observed in the unweighted and weighted survey participants, with the frequencies expected if the proportions had been the same as in the entire eligible population.
| Mental disorder | Sex | Age group (years) | Number in group | Frequency of any mental disorder | % (95% CI) | Unweighted Frequency | % (95% CI) | P value from Chi-squared test* | Weighted Frequency | % (95% CI) | P value from Chi-squared test* |
|-----------------|-----|------------------|----------------|---------------------------------|------------|---------------------|------------|--------------------------------|-------------------|------------|-------------------------------|
| Organic disorders | Females | 16–34 | 155,741 | NS | 3964 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
|                 | Males | 16–34 | 165,196 | NS | 3251 | 4722 | 0.15 (0.12–0.18) | 0.001 | 16 | 0.18 (0.15–0.21) | <0.001 |
|                 | 35–54 | 173,232 | 384 | 0.22 (0.20–0.24) | <0.001 | 34 | 0.20 (0.18–0.22) | <0.001 |
| Substance use disorders | Females | 16–34 | 155,741 | 1 | 0.95 (0.94–0.96) | 0.019 | 38 | 0.81 (0.79–0.83) | 0.184 |
|                 | Males | 16–34 | 165,196 | 115 | 2.00 (1.90–2.10) | <0.001 | 34 | 1.94 (1.84–2.04) | <0.001 |
|                 | 35–54 | 173,232 | 3990 | 2.00 (1.90–2.10) | <0.001 | 34 | 1.94 (1.84–2.04) | <0.001 |
| Schizophrenia | Females | 16–34 | 155,741 | 1662 | 1.07 (1.06–1.08) | 0.027 | 66 | 0.99 (0.96–1.01) | 0.103 |
|                 | Males | 16–34 | 165,196 | 1996 | 1.21 (1.19–1.23) | <0.001 | 34 | 1.19 (1.17–1.21) | <0.001 |
|                 | 35–54 | 173,232 | 2124 | 1.11 (1.09–1.13) | <0.001 | 34 | 1.10 (1.08–1.12) | <0.001 |
| Mood disorders | Females | 16–34 | 155,741 | 8168 | 5.24 (5.13–5.36) | <0.001 | 279 | 5.60 (5.50–5.70) | 0.002 |
|                 | Males | 16–34 | 165,196 | 4354 | 2.64 (2.54–2.74) | <0.001 | 127 | 2.60 (2.50–2.70) | <0.001 |
|                 | 35–54 | 173,232 | 7134 | 4.12 (4.02–4.23) | <0.001 | 127 | 3.98 (3.88–4.08) | <0.001 |
| Neurotic disorders | Females | 16–34 | 155,741 | 11890 | 7.63 (7.50–7.77) | <0.001 | 297 | 7.73 (7.62–7.84) | 0.008 |
|                 | Males | 16–34 | 165,196 | 4354 | 2.64 (2.54–2.74) | <0.001 | 127 | 2.60 (2.50–2.70) | <0.001 |
|                 | 35–54 | 173,232 | 7134 | 4.12 (4.02–4.23) | <0.001 | 127 | 3.98 (3.88–4.08) | <0.001 |
| Eating disorders | Females | 16–34 | 155,741 | 8168 | 5.24 (5.13–5.36) | <0.001 | 279 | 5.60 (5.50–5.70) | 0.002 |
|                 | Males | 16–34 | 165,196 | 4354 | 2.64 (2.54–2.74) | <0.001 | 127 | 2.60 (2.50–2.70) | <0.001 |
|                 | 35–54 | 173,232 | 7134 | 4.12 (4.02–4.23) | <0.001 | 127 | 3.98 (3.88–4.08) | <0.001 |
| Personality disorders | Females | 16–34 | 155,741 | 3269 | 2.1 (2.03–2.17) | <0.001 | 121 | 2.15 (2.08–2.23) | 0.031 |
|                 | Males | 16–34 | 165,196 | 4691 | 2.76 (2.69–2.84) | <0.001 | 123 | 2.70 (2.63–2.78) | 0.044 |
|                 | 35–54 | 173,232 | 3045 | 1.76 (1.70–1.82) | <0.001 | 123 | 1.70 (1.64–1.78) | <0.001 |
| Intellectual disabilities | Females | 16–34 | 155,741 | 987 | 0.63 (0.60–0.67) | <0.001 | 34 | 0.61 (0.58–0.64) | 0.001 |
|                 | Males | 16–34 | 165,196 | 2737 | 1.70 (1.63–1.77) | <0.001 | 34 | 1.66 (1.63–1.71) | <0.001 |
| Developmental disorders | Females | 16–34 | 155,741 | 987 | 0.63 (0.60–0.67) | <0.001 | 34 | 0.61 (0.58–0.64) | 0.001 |
|                 | Males | 16–34 | 165,196 | 2737 | 1.70 (1.63–1.77) | <0.001 | 34 | 1.66 (1.63–1.71) | <0.001 |

Continued.
| Mental disorder | Sex               | Number in group | Frequency of any mental disorder diagnosis | % (95% CI) | P value from Chi-squared test* | Frequency of any mental disorder diagnosis | % (95% CI) | P value from Chi-squared test* |
|-----------------|-------------------|-----------------|---------------------------------------------|------------|-------------------------------|---------------------------------------------|------------|-------------------------------|
|                 | Entire eligible population (n = 1,063,082) |                |                                             |            |                               |                                             |            |                               |
|                 | Survey participants (n = 32,417) |                |                                             |            |                               |                                             |            |                               |
|                 | Unweighted        | Weighted        |                                             |            |                               |                                             |            |                               |
| Behavioral disorders | Females 16–34 | 155,741          | 5381                                        | 3.46 (3.37–3.55) | 0.784                         | 182                                          | 3.83 (3.18–4.60) | 0.166                         |
|                  |                    |                  |                                             |            |                               |                                             |            |                               |
|                  | 35–54              | 169,769          | 1769                                        | 1.04 (0.99–1.09) | 0.142                         | 52                                           | 1.00 (0.73–1.38) | 0.768                         |
|                  |                    |                  |                                             |            |                               |                                             |            |                               |
|                  | 55+                | 207,897          | 247                                         | 0.12 (0.10–0.13) | 0.100                         | 17                                           | 0.27 (0.15–0.49) | <0.001                        |
|                  |                    |                  |                                             |            |                               |                                             |            |                               |
|                  | Males 16–34        | 165,106          | 9021                                        | 5.46 (5.35–5.57) | 0.158                         | 46                                           | 4.86 (4.09–5.73) | 0.053                         |
|                  |                    |                  |                                             |            |                               |                                             |            |                               |
|                  | 35–54              | 173,232          | 1462                                        | 1.42 (1.37–1.48) | 0.132                         | 33                                           | 1.11 (0.80–1.53) | 0.054                         |
|                  |                    |                  |                                             |            |                               |                                             |            |                               |
|                  | 55+                | 191,247          | 278                                         | 0.15 (0.13–0.16) | 0.100                         | 10                                           | 0.17 (0.08–0.38) | 0.648                         |

*Comparing the frequencies observed in the unweighted and weighted survey participants, with the frequencies expected if the proportions had been the same as in the entire eligible population.

NS: not shown – None of the frequencies, proportions and chi-squared tests for mental disorder types for a sex are shown if any of the age-groups comprised fewer than 5 cases.

Supplementary Table 7: Odds ratios and 95% confidence intervals for associations between any mental disorder and nine general medical conditions, among all those eligible for the 2017 Central Denmark Region and the How are you? survey participants (unweighted and weighted). Adjusted models were adjusted for sex, age group, and education.
Supplementary Figure 1: Frequency of diagnoses of types of mental disorders in specific sex- and age-groups within the eligible population in the Central Denmark Region and the How are you? sample (unweighted and weighted)

NB. None of the proportions for mental disorder types for a sex are shown if any of the age-groups comprised fewer than 5 cases.