A Comprehensive Nationwide Study of the Incidence Rate and Lifetime Risk for Treated Mental Disorders

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IMPORTANCE Understanding the epidemiologic profile of the life course of mental disorders is fundamental for research and planning for health care. Although previous studies have used population surveys, informative and complementary estimates can be derived from population-based registers.

OBJECTIVE To derive comprehensive and precise estimates of the incidence rate of and lifetime risk for any mental disorder and a range of specific mental disorders.

DESIGN, SETTING, AND PARTICIPANTS We conducted a follow-up study of all Danish residents (5.6 million persons), to whom all treatment is provided by the government health care system without charge to the patient, from January 1, 2000, through December 31, 2012 (total follow-up, 59.5 million person-years). During the study period, 320 543 persons received first lifetime treatment in a psychiatric setting for any mental disorder; 489 006 persons were censored owing to death; and 69 987 persons were censored owing to emigration. Specific categories of mental disorders investigated included organic mental disorders, substance abuse disorders, schizophrenia, mood disorders, anxiety, eating disorders, personality disorders, mental retardation, pervasive developmental disorders, and behavioral and emotional disorders.

EXPOSURES Age and sex.

MAIN OUTCOMES AND MEASURES Sex- and age-specific incidence rates and cumulative incidences and sex-specific lifetime risks.

RESULTS During the course of life, 37.66% of females (95% CI, 37.52%-37.80%) and 32.05% of males (31.91%-32.19%) received their first treatment in a psychiatric setting for any mental disorder. The occurrence of mental disorders varied markedly between diagnostic categories and by sex and age. The sex- and age-specific incidence rates for many mental disorders had a single peak incidence rate during the second and third decades of life. Some disorders had a second peak in the sex- and age-specific incidence rate later in life.

CONCLUSIONS AND RELEVANCE This nationwide study provides a first comprehensive assessment of the lifetime risks for treated mental disorders. Approximately one-third of the Danish population received treatment for mental disorders. The distinct signatures of the different mental disorders with respect to sex and age have important implications for service planning and etiologic research.
Understanding the life-course pattern of incidence rates and the magnitude of the lifetime risks for mental disorders are essential steps for rational planning of health care services. In addition, because incidence represents the force of morbidity in the population, variations in incidence of different mental disorders during a lifetime and between the sexes provide clues for understanding causes of the disorders. Community-based surveys have provided an important foundation for understanding the occurrence of common mental disorders. For example, the Epidemiologic Catchment Area Study estimated that 32% of the US population had a mental disorder at some time in their lives. Subsequent studies reported even higher lifetime prevalences of nearly 50% and 46.4%. Some reports have been greeted with skepticism, and others suggested that the community-based surveys included mild or transient disorders and false-positive cases of individuals with dramatic styles of personal presentation but little illness or impairment, thus inflating lifetime prevalences. Within the last decade, a European study estimated the lifetime prevalence of the range of mental disorders to be 26%.

Frequency estimates characterize the occurrence of disease in human populations and therefore are fundamental to descriptive and etiologic investigations. They enable us to describe how common an illness is in relation to the size of the population. Distinguishing between incidence, which reflects the number of new cases within a given time, and prevalence, which reflects the number of existing cases at a given point, is important. Incidence measures are typically estimated from cohort studies that involve follow-up of populations. For most chronic diseases, 1 person can experience a single onset throughout life. For recurrent diseases such as respiratory illnesses and including psychiatric disorders such as recurrent depression, we may wish to estimate incidence by assessing onsets that occur during a given period after recovery from an earlier episode. However, the first occurrence is often of greater interest than subsequent occurrences in the same individual, because that first occurrence may link more strongly to the hypothesized force of morbidity. In this report, we are studying first occurrences only.

Incidence rates of 1 or more mental disorders have been estimated by age and sex in population-based prospective surveys. However, the small number of incident cases, even with thousands of person-years of observation, introduced uncertainty in the estimated curves during the course of life. The sex- and age-specific incidence rate of disease occurrence is the instantaneous potential for change in disease status for each sex and age, relative to the sex- and age-specific size of the population. Others have referred to this concept as instantaneous risk, hazard, hazard rate, person-time incidence rate, first lifetime incidence rate, incidence, rate, and force of morbidity. The incidence rate refers to a population and has no easy interpretation on the individual level. However, having estimated sex- and age-specific incidence rates for the disorder of interest (and all competing events), sex- and age-specific cumulative incidences can be estimated readily. On the individual level, the cumulative incidence measures the probability of being affected with the disorder before a given age. Others have referred to this concept as incidence proportion, conditional probability, cumulative incidence function, cumulative incidence proportion, and risk. The cumulative incidence at a late age (eg, 100 years) is an estimate of a lifetime risk, whereas the prevalence is not. In addition, many studies failed to account for censoring owing to emigration and death, or they lacked the data.

Although lifetime risk estimates are useful for individual prediction of risk and assessment of societal burden, no previous study presented such estimates for a wide range of mental disorders. Because individuals with mental disorders have increased risks of death and emigration, the lifetime prevalence estimates of population-based surveys are underestimates of lifetime risks because they do not include persons who have emigrated or died before the time of the interview. The lifetime prevalence is sometimes called the proportion of survivors affected and has been estimated as the percentage of subjects in a survey who had the disorder before the interview. The lifetime risk allows estimation of the percentage of persons in the population who will develop the disorder before the end of their life. The lifetime prevalence estimates the proportion of survivors with the disease, whereas the lifetime risk estimates the probability of having the disorder throughout life.

Epidemiologic techniques are available to derive lifetime risks based on population-based health registers. Nationwide mental health registers with unique personal identifiers are available in some developed nations now, but in general these registers have not been suitable for estimating lifetime risks, because they have not been in operation long enough to capture the entire lifetime, and because many registers are not representative of the general population. The few studies that have used health registers have focused on only single disorders. We undertook a comprehensive study of the lifetime risk for mental disorders treated in secondary care settings—that is, a psychiatric hospital, specialty psychiatric clinic, or emergency department—based on the entire Danish population. In Denmark, medical treatment is provided by the government health care system without charge to the patient, with national and prospective registration for all individuals in secondary care since 1969. We estimated sex- and age-specific incidence rates and cumulative incidences for a wide range of mental disorders. The incidence rate measures the number of persons treated for the first time in their life per 10 000 person-years at risk. The cumulative incidence measures the expected percentage of persons in the population who will be treated for the disorder before a given age. We defined the lifetime risk as the cumulative incidence at the 100th birthday. Because we use competing risk survival analyses, persons need not to be alive at the 100th birthday to contribute to the estimation of the lifetime risk.

Methods

Study Population
The Danish Civil Registration System was established in 1968, when all people alive and residing in Denmark were regis-
tered. At present, 5.6 million persons live in Denmark. From 1968 onward, the system includes the personal identification number, sex, date of birth, and continuously updated information on vital status. The personal identification number is used in all national registers, enabling accurate linkage between registers and avoiding duplication of prior episodes occurring anywhere else in the nation. Our study population included all persons born in Denmark from January 1, 1900, through December 31, 2010.

This study was approved by the Danish Data Protection Agency. By Danish law, informed consent is not required for register-based studies.

Assessment of Mental Illness
The study population was linked with the Danish Psychiatric Central Research Register30 to obtain information on mental illness treated in secondary care. From 1969 the Danish Psychiatric Central Register contained data on all admissions to Danish psychiatric inpatient facilities; from 1995, information on all contacts to outpatient psychiatric departments and visits to psychiatric emergency care units was included. Denmark has no private psychiatric hospitals, and all visiting patients are registered in the Danish Psychiatric Central Research Register. From 1969 to 1993, the diagnostic system used was the Danish modification of the International Classification of Diseases, 8th Revision (ICD-8)31; from 1994, the ICD-10 Classification of Mental and Behavioural Disorders: Diagnostic Criteria for Research (ICD-10-DCR).32 Individuals were classified with a mental disorder if they had been admitted to a psychiatric hospital, received outpatient psychiatric care, or visited a psychiatric emergency care unit. The spectrum of specific mental disorders considered is shown in Table 1. Individuals with more than 1 disorder were included in the numerator for each specific disorder. For each mental disorder, the date of onset was defined as the first day of the first contact (inpatient, outpatient, or psychiatric emergency care unit), given the diagnosis of interest.

Study Design
Persons were followed up from January 1, 2000, or the earliest age at which a person might possibly develop the specific disorder (Table 1), whichever came later. Follow-up was terminated at the first treatment of the disorder, death, emigration from Denmark, or December 31, 2012, whichever came first. The findings were based on putative incident cases diagnosed according to the ICD-10-DCR classification system during a period when inpatient and outpatient information was included in the register. To reduce the risk that prevalent cases with access to services before the period of observation (ie, before 2000) were misclassified as incident cases, we excluded individuals who had been diagnosed using the ICD-8 classification and/or during the first 6 years of the operation of the ICD-10-DCR system. This stringent washout rule meant that our incident cases could not have previously accessed services for the psychiatric condition of interest for a 31-year period from 1969 through 1999. This procedure was used for each disorder separately. Sensitivity analyses that extended the washout period to 36 years revealed nearly identical results.

We included only persons who were alive and resided in Denmark at initiation of follow-up to control for possible increased risk for mental disorders associated with immigration.34,35

Statistical Analysis
We estimated sex- and age-specific incidence rates and cumulative incidences of the first occurrence of any psychiatric disorder (ICD-8 codes 290-315; ICD-10-DCR codes F00-F99) and a number of separate mental disorders (Table 1). The incidence rate measures the number of persons treated for the first time in their life per 10 000 person-years at risk, and the cumulative incidence measures the percentages of persons in the population who will be treated for the disorder before a given age. We define the lifetime risk as the cumulative incidence at the 100th birthday. Cumulative incidences were calculated for each sex and mental disorder separately and were estimated using competing risk survival analyses to account for the fact that persons are simultaneously at risk for a mental disorder, death, or emigration from Denmark. Ignoring censoring from emigration and/or death will bias the estimated incidence rates downward and the estimated cumulative incidences upward.22 Because we use competing risk survival analyses, persons need not be alive at their 100th birthday to contribute to the estimation of the lifetime risk. The 100th birthday was chosen to ensure that disorders from birth throughout the entire life course were enumerated.

Results
The cohort of 5.6 million Danish residents was followed up for 59.5 million person-years; the longest individual follow-up was 13 years (2000-2012). A total of 320 543 persons had their first psychiatric contact for any psychiatric disorder during follow-up; 489 006 persons were censored owing to death; and 69 987 persons were censored owing to emigration from Denmark.

The lifetime risk for any psychiatric disorder was 37.66% for a female and 32.05% for a male (Table 2). Table 2 also shows the probability of having a psychiatric contact for each disorder before 50 years of age.

Figure 1, Figure 2, and the Supplement (eFigures 1 to 5) show the sex- and age-specific incidence rates and cumulative incidences for any psychiatric disorder and the specific psychiatric disorders investigated. These incidence curves display differences that may be regarded as epidemiologic signatures and suggest clues to causes that may be connected to particular periods of the life course. For example, organic mental disorders (Figure 1A) showed an onset late in life for which both sexes had almost identical age-specific incidence rates. That similarity can be compared with the sharp rise in incidence rate of psychoactive substance abuse disorders from 10 to 20 years of age, then a drop until about 30 years of age (Figure 1B). Females had a rise with a second peak at about 45 years of age and then a decline thereafter. The probability of first treatment for any disorder from, for example, 20 to 40 years of age, is estimated as the cumulative incidence at age 40 years minus the cumulative incidence at age 20 years.
Both sexes had almost identical incidence rates and cumulative incidences for schizophrenia during childhood and adolescence, but from 20 to 50 years of age, males had higher incidence rates and cumulative incidences (Figure 1C). We found some indication that after 50 years of age, females had higher incidence rates than males, which became more promi-

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>ICD-10-DCR Codes*</th>
<th>Equivalent ICD-8 Codes</th>
<th>Earliest Possible Age at Onset, y</th>
<th>No. of Prevalent Cases Before Follow-up</th>
<th>No. of Persons at Risk at Initiation of Follow-up</th>
<th>No. of New Cases During Follow-up</th>
</tr>
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<tr>
<td>Any psychiatric disorder</td>
<td>F00-F99</td>
<td>290-315</td>
<td>1</td>
<td>249 956</td>
<td>5 364 461</td>
<td>320 543</td>
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<td>Organic, including symptomatic, mental disorders</td>
<td>F00-F09</td>
<td>290.09, 290.10, 290.11, 290.18, 292.x9, 293.x9, 294.x9, 309.x9</td>
<td>35</td>
<td>24 001</td>
<td>3 508 367</td>
<td>66 539</td>
</tr>
<tr>
<td>Dementia in Alzheimer disease</td>
<td>F00</td>
<td>290.09, 290.10, 290.19</td>
<td>35</td>
<td>6109</td>
<td>3 526 259</td>
<td>25 756</td>
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<tr>
<td>Vascular dementia</td>
<td>F01</td>
<td>293.09, 293.19</td>
<td>35</td>
<td>3059</td>
<td>3 529 309</td>
<td>11 865</td>
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<tr>
<td>Mental and behavioral disorders due to psychoactive substance abuse</td>
<td>F10-F19</td>
<td>291.x9, 294.39, 303.x9, 303.20, 303.28, 303.90, 304.x9</td>
<td>10</td>
<td>66 352</td>
<td>4 965 624</td>
<td>53 645</td>
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<tr>
<td>Mental and behavioral disorders due to alcohol use</td>
<td>F10</td>
<td>291.x9, 301.x9, 303.20, 303.28, 303.90</td>
<td>10</td>
<td>51 986</td>
<td>4 979 990</td>
<td>37 332</td>
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<td>Mental and behavioral disorders due to cannabis use</td>
<td>F12</td>
<td>304.59</td>
<td>10</td>
<td>6114</td>
<td>5 025 862</td>
<td>12 179</td>
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<td>Schizophrenia and related disorders</td>
<td>F20-F29</td>
<td>295.x9, 296.89, 297.x9, 298.29-298.99, 299.04, 299.05, 299.09, 301.83</td>
<td>10</td>
<td>45 610</td>
<td>4 986 366</td>
<td>30 217</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>F20</td>
<td>295.x9 (excluding 295.79)</td>
<td>10</td>
<td>19 713</td>
<td>5 012 263</td>
<td>14 364</td>
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<td>Schizoaffective disorder</td>
<td>F25</td>
<td>295.79, 296.89</td>
<td>10</td>
<td>4460</td>
<td>5 027 516</td>
<td>2442</td>
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<td>Mood disorders</td>
<td>F30-F39</td>
<td>296.x9 (excluding 296.89, 296.09, 296.19, 304.49, 301.19)</td>
<td>10</td>
<td>73 873</td>
<td>4 958 103</td>
<td>113 565</td>
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<td>Bipolar disorders</td>
<td>F30-F31</td>
<td>296.19, 296.39, 296.19</td>
<td>10</td>
<td>12 664</td>
<td>5 019 312</td>
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<td>Recurrent depressive disorder</td>
<td>F33</td>
<td>296.09, 296.29, 298.09, 300.49*</td>
<td>10</td>
<td>22 362</td>
<td>5 009 614</td>
<td>48 532</td>
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<td>Single and recurrent depressive disorder</td>
<td>F32-F33</td>
<td>296.09, 296.29, 298.09, 300.49</td>
<td>10</td>
<td>62 795</td>
<td>4 969 181</td>
<td>105 108</td>
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<tr>
<td>Neurotic, stress-related, and somatoform disorders</td>
<td>F40-F48</td>
<td>300.x9 (excluding 300.49, 305.x9, 305.68, 307.99)</td>
<td>5</td>
<td>89 213</td>
<td>5 261 721</td>
<td>139 929</td>
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<td>Obsessive-compulsive disorder</td>
<td>F42</td>
<td>300.39</td>
<td>5</td>
<td>2506</td>
<td>5 348 428</td>
<td>10 242</td>
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<tr>
<td>Eating disorders</td>
<td>F50</td>
<td>305.60, 306.50, 306.58, 306.59</td>
<td>1</td>
<td>5176</td>
<td>5 609 241</td>
<td>12 480</td>
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<tr>
<td>Anorexia nervosa</td>
<td>F50.0</td>
<td>306.50</td>
<td>1</td>
<td>2096</td>
<td>5 612 321</td>
<td>3673</td>
</tr>
<tr>
<td>Specific personality disorders</td>
<td>F60</td>
<td>301.x9 (excluding 301.19, 301.80, 301.81, 301.82, 301.84)</td>
<td>10</td>
<td>71 965</td>
<td>4 960 011</td>
<td>41 477</td>
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<tr>
<td>Borderline-type</td>
<td>F60.31</td>
<td>301.84</td>
<td>10</td>
<td>6636</td>
<td>5 025 340</td>
<td>9265</td>
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<tr>
<td>Mental retardation</td>
<td>F70-F79</td>
<td>311.xx, 312.xx, 313.xx, 314.xx, 315.xx</td>
<td>1</td>
<td>5560</td>
<td>5 608 857</td>
<td>12 703</td>
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<tr>
<td>Pervasive developmental disorders</td>
<td>F84</td>
<td>299.00, 299.01, 299.02, 299.03</td>
<td>1</td>
<td>3270</td>
<td>5 611 147</td>
<td>16 824</td>
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<tr>
<td>Childhood autism</td>
<td>F84.0</td>
<td>299.00</td>
<td>1</td>
<td>828</td>
<td>5 613 589</td>
<td>4725</td>
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<tr>
<td>Behavioral and emotional disorders with onset usually occurring in childhood and adolescence</td>
<td>F90-F98</td>
<td>306.x9, 308.x</td>
<td>1</td>
<td>13 807</td>
<td>5 600 610</td>
<td>44 473</td>
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<tr>
<td>Hyperkinetic disorder</td>
<td>F90</td>
<td>308.01</td>
<td>1</td>
<td>2522</td>
<td>5 611 895</td>
<td>27 699</td>
</tr>
</tbody>
</table>

Abbreviations: ICD-8, International Classification of Diseases. 8th Revision; ICD-10-DCR, ICD-10 Classification of Mental and Behavioural Disorders: Diagnostic Criteria for Research.

* Inclusive of diagnostic categories for which a valid conversion to the ICD-8 code was possible.

b For recurrent depression, onset was defined as the second admission that occurred at least 8 weeks after last discharge with these ICD-8 codes.

Both sexes had almost identical incidence rates and cumulative incidences for schizophrenia during childhood and adolescence, but from 20 to 50 years of age, males had higher incidence rates and cumulative incidences (Figure 1C). We found some indication that after 50 years of age, females had higher incidence rates than males, which became more promi-
Sex and age-specific incidence rates and cumulative incidences for any psychiatric disorder and for all 25 specific disorders investigated are available on the authors’ web site (http://ncrr.au.dk/en/publications). These estimates are identical to those presented in Table 2, Figures 1 and 2, and the Supplement (eFigures 1-5).

Discussion

Based on the present findings, one-third of the Danish population will receive treatment in secondary care for a mental disorder across their lifetime. The incidence rates and cumulative incidence of mental disorders vary markedly between the sexes and across the range of ages. As expected, we found major sex differences in certain disorders. Males were more likely to receive treatment for disorders such as autism, mental retardation, hyperkinetic disorders, schizophrenia, and substance use disorders, whereas women were more likely to receive treatment for anxiety, mood disorders, and eating disorders. We estimate that 3.67% of females and 3.78% of
Males received treatment for schizophrenia and related disorders (Table 2) and that 15.50% and 9.07% of females and males, respectively, received treatment for depression. Neurotic, stress-related, and somatoform disorders (females, 18.97%; males, 12.51%); mood disorders (females, 16.48%; males, 9.95%); and organic mental disorders (females, 11.98%; males, 8.48%) had highest lifetime risks for both sexes (Table 2). However, the World Mental Health Surveys\(^6\) were 9.8% to 15.8% and 4.8% to 9.6%, respectively, which are in the same range of the estimates from the present study.

Most mental disorders have their peak age at onset in the first and second decades of life, whereas organic disorders like dementia have late onset. Mood disorders had a bimodal age distribution,\(^{35}\) with peaks in the early third and in the ninth decades of life suggesting the possibility of differing causes.\(^{37}\)

The bimodal distribution for disorders of substance abuse suggests that different substances may be abused (eg, marijuana and cocaine in youth and alcohol in older adults).

Although lifetime prevalences and lifetime risks are not directly comparable, our overall estimates for treated lifetime risks for mental disorders are somewhat lower than US-based community surveys\(^1\) that have found lifetime prevalence ranging from 40% to 50%. In the World Mental Health Survey Initiative,\(^4\) the interquartile range for the lifetime prevalence of any mental disorder was 12% to 47%, thus capturing 15.50% for males and 37.66% for females. For mood and substance use disorders, the interquartile ranges from the World Mental Health Surveys\(^6\) were 9.8% to 15.8% and 4.8% to 9.6%, respectively, which are in the same range of the estimates in Table 2. However, the World Mental Health Surveys and the US surveys included a spectrum of common mental disorders, whereas we were able to include a broader range of mental disorders and childhood psychiatric disorders.

The risk estimates of mental disorders in a given population are influenced by the study design, which affects the validity and the generalizability of the results. Register-based studies such as the present one cannot capture persons with untreated disorders; however, population-based surveys can.
derived diagnoses have several strengths (eg, access to mental health records, details from family members and key informants, and overall clinical judgment) but may lack the reliability that can be obtained by well-trained interviewers using standardized diagnostic interviews. Although systematic studies validating all clinical diagnoses presented in this study are not available, many of the key diagnoses (ie, schizophrenia, a single depressive episode, affective disorder, dementia, and autism) have been validated with good results. The contrast-
tered in the Danish Psychiatric Central Register. However, if they visit a psychiatric inpatient or outpatient clinic or a psychiatric emergency care unit for their disorders, these patients will be registered, albeit with a delayed age of onset. Therefore, the age-specific pattern for the severe mental disorders likely represents the true age-specific incidence of the disorder, whereas the age-specific pattern for the less severe disorders may show a delayed age-specific pattern of the disorder.

Despite this conservative bias of our approach, the overall estimate of lifetime risk is close to the lifetime prevalences presented in community surveys. The early onset for many mental disorders, combined with other information on disability and chronicity of mental disorders, helps to explain the sizable burden of disability-adjusted life-years attributable to mental disorders.50

As with any other study of health-related outcomes, our estimates may be biased by birth cohort effects (eg, differences in prenatal care, differences in childhood vaccination schedules). No evidence of birth cohort effects exists during the ICD-10-DCR period for the disorders studied, except for autism.28

The novelty of this report is the comprehensive nationwide assessment of lifetime risks, sex- and age-specific incidence rates, and sex- and age-specific cumulative incidences of mental disorders treated in secondary care during a full lifetime. The curves for anorexia and the similarity in males and females for schizophrenia are novel. Bimodalities in the lifelong course patterns of mood and substance use disorders have occasionally been reported, but never with such high precision. The distinct signatures of the different mental disorders have important implications for service planning and etiologic research. With respect to service planning, our register-based findings should guide allocation of future health care funding in terms of total demand estimated over the lifetime, the age distributions expected at different treatment facilities, and the ages at which primary prevention activities are targeted. The incidence rates confirm that a large proportion of mental disorders reach secondary care during the second and third decades of life, consistent with the renewed focus on the global public health needs of young people.27 At the other extreme of life, our estimates provide a stark reminder about the steep rise in the onset of mental disorders after 60 years of age, including late-occurring mood disorders and Alzheimer disease.

Conclusions

This nationwide study provides a first comprehensive assessment of the lifetime risks for treated mental disorders. The distinct signatures of the different mental disorders with respect to sex and age have important implications for service planning and etiologic research.
Rate of and Risk for Mental Disorders in Denmark

Original Investigation

Research

27. Thorup A, Wolfrat BL, Pedersen CB, Mortensen PB, Nordenfelt M. Young males have a higher risk of developing schizophrenia: a Danish register study. Psychol Med. 2007;37(4):479-484.