Supplemental Online Content

Kessing LV, Ziersen SC, Caspi A, Moffitt TE, Andersen PK. Lifetime incidence of treated mental health disorders and psychotropic drug prescriptions and associated socioeconomic functioning. *JAMA Psychiatry*. Published online July 12, 2023. doi:10.1001/jamapsychiatry.2023.2206

This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix 1: Description of inclusion and exclusion diagnostic criteria

Inclusion ICD-10 codes for individual mental disorders from 1. January 1994 and corresponding excluding ICD-8 codes from January 1, 1971 to 31.12.1993.

Use of alcohol or psychoactive drugs (F10-19), *exclusion criteria*: ICD-8: 291 Alcoholic psychosis, 303 Alcoholism, 304 Drug dependence.
Schizophrenia and related disorders (F20-29), *exclusion criteria*: ICD-8: 295 Schizophrenia, 297

Paranoid states, 298 Other psychoses, 299 Unspecified psychosis.

Bipolar disorder (F30-31.9+34.0+38.0), *exclusion criteria*: ICD-8: 296.19, 296.39.

Unipolar disorder (F32-33.9+34.1+38.10), *exclusion criteria*: ICD-8: 296.09, 296.29.

Neurotic, stress-related and somatoform disorder (F40-48.9), *exclusion criteria*: ICD-8: 300

Neuroses.

Eating disorders (F50-50.9), *exclusion criteria*: ICD-8: 306.50, 306.58, 306.59.

Other behavioral syndromes associated with physiological disturbances and physical factors (F51-

59), *exclusion criteria*: ICD-8: 309.

Personality disorders (F60-69), *exclusion criteria*: ICD-8: 301 Personality disorders.

Disorders of psychological development and disorders with onset usually in childhood and

adolescence (F80-98.9), *exclusion criteria*: ICD-8: 299.00-299.03 (psychosis infantilis) + child

mental disorders, non-psychotic: 308-308.99

Other psychiatric disorders (F70-79+F99)

eAppendix 2: Description of psychotropic medication included and not included in the analyses

Included medication

1) antipsychotics (N05A minus N05AN), 2) antidepressants (N06A), 3) lithium (N05AN), 4) anxiolytics (N05B excluding benzodiazepine derivatives (N05BA01: diazepam)), 5) medication for ADHD (C02AC02, N06BA02, N06BA04, N06BA09 and N06BA12) and 6) medication for alcohol and opioid dependence (ATC code N07BB-N07BB04).

Not included medication

As we did not want to overestimate mental disorder, we did not include the following medications: hypnotics for sleep (N05C), medication for dementia (N06D), parasympatomimetics (N07A, prescribed for neurological disorders) or medication for smoking cessation (nicotine dependence, N07BA) or the following diagnoses: dementia, delirium and other organic related mental disorders (F00-09).

eAppendix 3: The Aalen-Johansen estimator of lifetime risk

The starting point for the Aalen-Johansen estimator of lifetime risk is the classical multiple decrement life-table estimator from demography (e.g., S. H. Preston, P. Heuveline, M. Guillot: 'Demography - Measuring and Modeling Population Processes', Blackwell, 2001, chapter 4). In the multiple decrement life-table, observations are viewed in a Lexis diagram, i.e., a calendar time by age coordinate system; see Figure 3S. In the present study, subjects enter at 1 Jan 1996 where they are between 1 and 100 years old and they are followed, at most, until the end of study in 2018 but subjects may leave the study prior to that date if they die or acquire Any mental disorder, if they turn 100 years or if they emigrate. Based on the follow-up of the subjects, age-specific disease and death rates can be computed in suitable intervals as indicated by horizontal strips in the Lexis diagram. Table 3S shows the basis for these rates; i.e., numbers of cases of Any mental disorder and deaths together with person-years at risk in 10-year age intervals. The resulting rates are then combined into an estimate of the age-specific cumulative incidence; i.e. the risk of Any mental disorder at the end of the age intervals, resulting in the lifetime risk at the end of the final interval (100 years). The estimated cumulative incidence of Any mental disorder based on the life-table is also shown in the table.

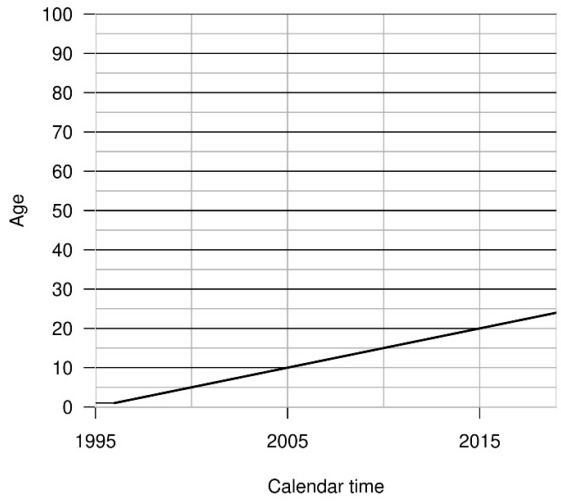
The Aalen-Johansen estimator is a modern ‘continuous-time version’ of the life-table estimator that is obtained, intuitively, by letting the age intervals become shorter and shorter and has, thus, the advantage that no age intervals need to be chosen. However, as seen in Table 3S and in Supplement 3, the two estimators provide results that are very close. Both estimate the lifetime risk of Any mental disorder in a ‘synthetic’ birth cohort followed until age 100 in which the age-specific rates of Any mental disorder and death are as estimated. The explanation of why roughly 450,000 cases of Any mental disorder out of roughly 1,300,000 subjects can yield an estimated lifetime risk of 0.83 is that the lifetime risk very much depends on the timing of the cases in relation to the ages at

which subjects are at risk. The Aalen-Johansen estimator is described by Andersen et al. (Andersen, P.K., Geskus, R.B., de Witte, T., Putter, H., 2012, 'Competing risks in epidemiology: Possibilities and pitfalls.', Int. J. Epidemiol., 41, 861-870).

Table 3S. Numbers of cases of Any mental disorder and deaths.

Age	Person-years at risk		Events	Deaths	Cumulative incidence of Any mental disorder
[0,10)	584229.4		1947	58	0.033
[10,20)	2091650.9		24670	478	0.140
[20,30)	3064983.2		61074	921	0.295
[30,40)	3330732.3		69058	1387	0.426
[40,50)	3358989.5		73699	3336	0.537
[50,60)	3121618.9		68820	8830	0.624
[60,70)	2466306		55331	19631	0.692
[70,80)	1567250		56734	34934	0.763
[80,90)	678539.9		41744	43537	0.814
[90,100)	112635.7		9545	19789	0.826

Figure 3S: Lexis diagram of calendar time by age coordinate system together with person-years at risk in 10-year age intervals



eAppendix 4: Description of definitions and statistical analyses of socio-economic measures

Educational achievement, employment, and income were measured from the start of adulthood at age 18 years (as defined according to Danish law) and up to age 67 years (age for public retirement pension). Residential and marital status were measured from age 18 years up to age 100 years. Educational achievement, employment, income, residential status, and marital status were assessed at baseline, i.e., at the date of the diagnosis/treatment of the mental disorder, and the four latter outcomes were also assessed during follow-up.

For the baseline analyses at the date of the diagnosis/treatment of the mental disorder, we calculated the risk of a "poor" outcome (i.e., low education, unemployment/disability, low income, not cohabiting, not married) for patients and for controls, and the differences between patients and controls, together with the corresponding 95% confidence interval.

For the follow-up analyses, we estimated the hazard ratio (HR) of time to switch from not having a poor outcome at baseline to a poor outcome at follow-up, for patients compared to control individuals from the general population matched according to the inclusion date, year of birth, and sex.

eTable 1: Cumulative incidences according to age and gender. The table shows cumulative incidence according to age and gender for patients with 1) Any mental disorder, 2) any hospital-contact mental-disorder diagnosis, and 3) any psychotropicmedication without prior hospital-contact related to mental disorder.

	Any mental disorder			Any hospital-contact mental-disorder diagnosis			Any psychotropic medication without prior hospital-contact related to mental disorder		
	Total	Male	Female	Total	Male	Female	Total	Male	Female
Age (years)									
< 20	0.120	0.109	0.30	0.077	0.074	0.079	0.061	0.051	0.072
< 40	0.412	0.362	0.464	0.194	0.176	0.213	0.307	0.261	0.355
< 60	0.616	0.552	0.678	0.250	0.230	0.271	0.501	0.440	0.561
< 80	0.761	0.702	0.815	0.277	0.253	0.301	0.644	0.587	0.696
< 100	0.825	0.767	0.875	0.290	0.261	0.318	0.704	0.651	0.756

eAppendix 5: Sensitivity analysis of the cumulative incidences of "any hospital-contact mental-disorder diagnosis or any psychotropic medication" according to length of the exclusion period.

Question: Do the cumulative incidences of mental disorder vary systematically with length of the exclusion period or start of the study period?

Analyses at Study start at 2000 and 2005, respectively

We estimated the cumulative incidence of any hospital-contact mental disorder or any psychotropic medication (= any mental disorder) from 2000 and 2005, respectively, to 2018. For each specific start date, patients were excluded based on prior purchases of psychotropic medication (between 1995 and 2000 or between 1995 and 2005, respectively).

Legend to Figure 5AS: cumulative incidence of any mental disorder based with study start in 2000-01-01.

Legend to Figure 5BS: cumulative incidence of any mental disorder based with study start in 2005-01-01.

"Subjects" below the X axis refers to the number of individuals at risk at age 20, 40, 60 and 80 years.

Figure 5AS

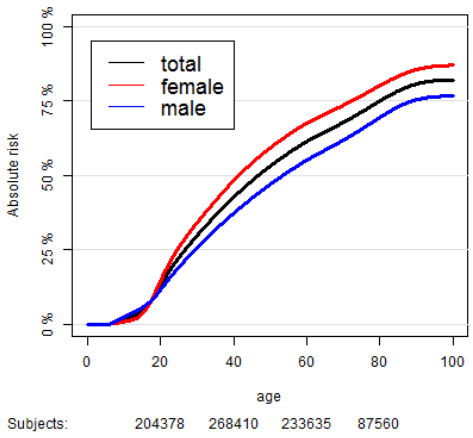


Figure 5BS

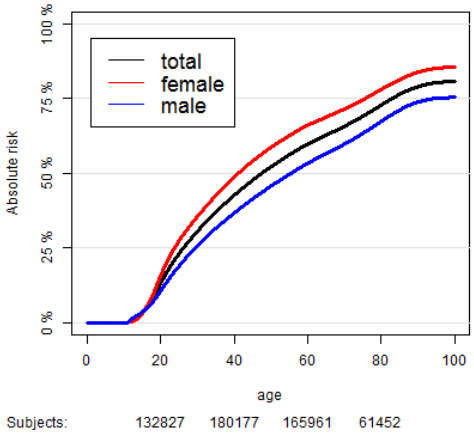
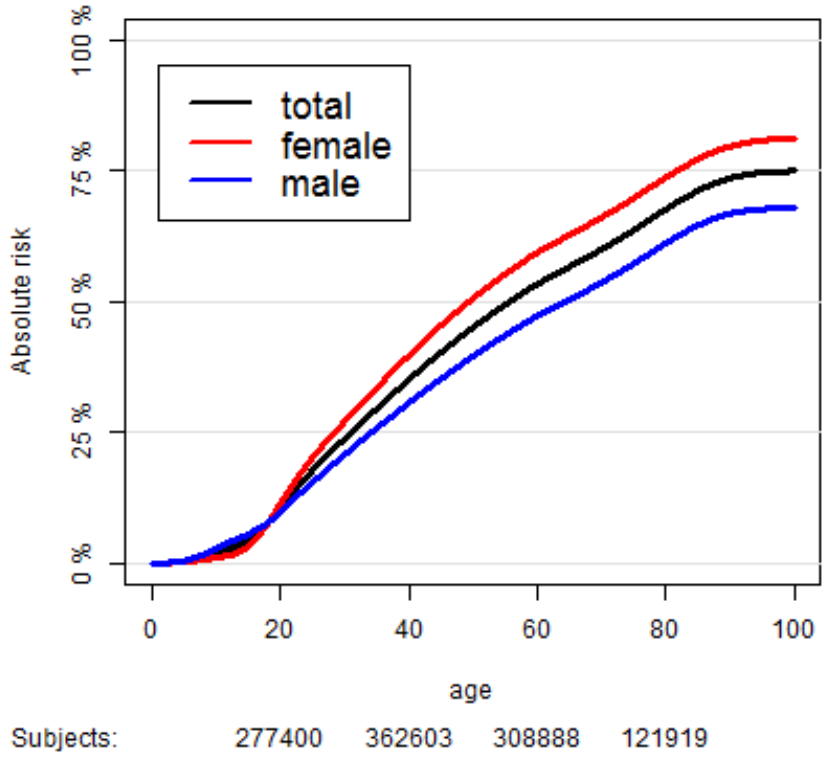


Table 5S: cumulative incidences of any hospital-contact mental disorder or any psychotropic medication (= any mental disorder) starting in 2000 and 2005, respectively.

	Start date: 2000-01-01	Start date: 2005-01-01
Age (years)		
20	0.129 (0.127, 0.131)	0.130 (0.127, 0.133)
40	0.426 (0.424, 0.428)	0.425 (0.423, 0.428)
60	0.613 (0.611, 0.615)	0.597 (0.595, 0.599)
80	0.750 (0.748, 0.751)	0.728 (0.726, 0.729)
100	0.820 (0.819, 0.821)	0.806 (0.804, 0.807)

Conclusion: The cumulative incidences of mental disorder did not consistently vary with length of the exclusion period or start of the study period.

eFigure: Sensitivity analysis of the cumulative incidences of "any hospital-contact mental-disorder diagnosis or any psychotropic medication prescribed at least two times". The figure shows the cumulative incidences from birth to age 100 years of any mental disorder estimated as "any hospital-contact mental-disorder diagnosis or any psychotropic medication prescribed at least two times".
"Subjects" below the X axis refers to the number of individuals at risk at age 20, 40, 60 and 80 years.



eTable 2: Cumulative incidences according to age for different psychotropics

	Antidepressants	Anxiolytics	Antipsychotics	ADHD-medication	Lithium	Alcohol and opioids treatment
Age (years)						
20	0.051	0.044	0.020	0.014	0	0.002
40	0.294	0.191	0.101	0.036	0.005	0.036
60	0.488	0.372	0.174	0.044	0.011	0.082
80	0.629	0.539	0.259	0.047	0.015	0.096
100	0.696	0.615	0.333	0.048	0.015	0.097

eAppendix 6: Analysis of cumulative incidences according to calendar time.

As there is a general belief that the incidence of mental disorder is continuing to increase with calendar time, time trends were explored.

Question: Do incidences of "any hospital-contact mental disorder" and "any mental disorder or any psychotropic medication (= Any mental disorder)" increase with calendar time?

Time trend analyses: The period 1996-01-01 to 2018-01-01 was divided into four intervals equal in length corresponding to 2009 days. The cumulative incidence function was estimated for each period from age 3*2009/365.25 = 16.5 to 100 to make comparison of periods possible.

Legend to Figure 6AS: Cumulative incidence of any hospital-contact mental disorder from age 16.5 to 100 for four different time periods. 1: 1996-01-01 + 2009 days, 2: 1996-01-01 + 4018 days, etc.
Legend to Figure 6BS: Cumulative incidence of any mental disorder from age 16.5 to 100 for four different time periods. 1: 1996-01-01 + 2009 days, 2: 1996-01-01 + 4018 days, etc.
Numbers below the Figures refer to the number of individuals at risk at age 20, 40, 60 and 80 years.

The curves start at age 16.5 years as data on younger individuals for recent study periods are not available, and cumulative incidence curves from birth would consequently not be comparable.

Figure 6AS

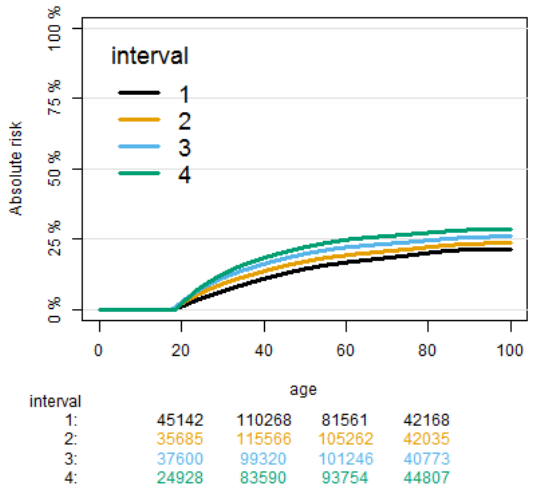
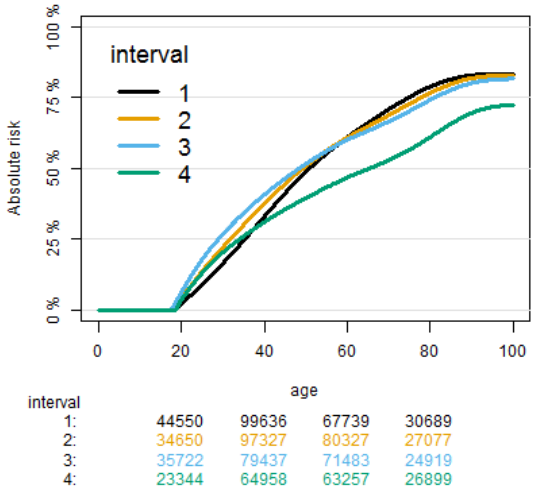


Figure 6BS



Age 100 years	**Any hospital-contact mental disorder diagnosis % (95%CI)**	**Any mental disorder % (95%CI)**
Interval		
1 (first)	21.6 (21.3, 21.9)	83.5 (83.4, 83.7)
2	23.6 (23.3, 24.0)	83.0 (82.8, 83.1)
3	26.0 (25.6, 26.3)	81.7 (81.4, 81.9)
4 (last)	28.6 (28.2, 29.1)	72.5 (72.1, 72.8)

Conclusion: The incidence of "any hospital-contact mental disorder" increased with calendar time while the incidence of "Any mental disorder (which includes prescriptions of psychotropics)" decreased with calendar time.