

1 The impact of social distancing on mental health during the Covid-19
2 pandemic: A nationwide study of 4.6 million Danish adults
3

4 Andreas Geest¹, Barbara Bonnesen¹, Alexander Jordan¹, Louise Tønnesen¹, Valdemar Rømer¹,
5 Charlotte S. Ulrik^{1,2}, Zitta Barrella Harboe^{3,5}, Josefin Eklöf¹, Pradeesh Sivapalan^{1,5}, Jens-Ulrik
6 Stæhr Jensen^{1,4,5}

7
8 ¹ Copenhagen Respiratory Research (COP:RESP), Department of Internal Medicine, Herlev-Gentofte University
9 Hospital, Hellerup, Denmark

10 ²Department of Respiratory Medicine, Copenhagen University Hospital – Hvidovre, Denmark

11 ³Department of Pulmonary and Infectious Diseases, University Hospital of Copenhagen, North Zealand, Denmark

12 ⁴Center for Health and Infectious Diseases Research (CHIP), University Hospital of Copenhagen, Copenhagen,
13 Denmark

14 ⁵Department of Clinical Medicine, Faculty of Health Sciences, University of Copenhagen, Copenhagen Denmark.
15

16 Corresponding Author

- 17 • Name: Andreas Geest (AG)
- 18 • Address: Aebeløgade 26, 3tv, 2100 Copenhagen, Denmark
- 19 • E-mail: Andreas.geest@regionh.dk

20 Work should be attributed:

- 21 • Department of Internal Medicine, Section of Respiratory Medicine, Herlev- Gentofte
22 University Hospital, Denmark

23 Shortened title:

This peer-reviewed article has been accepted for publication but not yet copyedited or typeset, and so may be subject to change during the production process. The article is considered published and may be cited using its DOI.

This is an Open Access article, distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives licence (<http://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is unaltered and is properly cited. The written permission of Cambridge University Press must be obtained for commercial re-use or in order to create a derivative work.

- 24 • Social distancing and the impact on mental health during the Covid-19 pandemic.

25 Keywords:

- 26 • Covid-19, Pandemic, Mental health, Pulmonary Disease, Epidemiology

27 Abstract

28 Background

29 Current knowledge on psychiatric illness following periods of social distancing during the COVID-
30 19 pandemic is mostly limited to smaller studies in selected populations. This nationwide study of
31 all 4.6 million Danish adults examined if periods of social distancing were associated with changes
32 in surrogate measures of mental health.

33 Methods

34 All Danish adults (≥ 18 years) were included and rates of collection of antidepressant prescriptions,
35 psychiatric hospital admission and suicide or suicide attempt for the periods March 12, 2020 – May
36 20, 2020 (lockdown period 1), and December 21, 2020 – March 1, 2021 (lockdown period 2), were
37 compared to corresponding periods one year prior. Individuals were censored due to death or
38 SARS-CoV-2 infection.

39 Results

40 Rates of antidepressant consumption were increased for both period 1 and 2, with an IRR of 1.02
41 (95% CI 1.01-1.02, $p < 0.001$) and IRR of 1.08 (95% CI 1.08-1.09, $p < 0.001$), respectively,
42 compared to the control periods. Rates of psychiatric hospital admissions decreased significantly
43 with an IRR of 0.65 (95% CI 0.63-0.66, $p < 0.001$) for period 1 and 0.86 (95% CI 0.84-0.88 $p <$
44 0.001) for period 2. The risk of suicide was not increased in period 1, IRR 0.96 (95% CI 0.82-1.13,
45 $p = 0.64$), but seemed increased in period 2, IRR 1.19 (95% CI 1.02-1.38, $p = 0.03$).

46 Conclusion

47 Periods of social distancing during Covid-19 were associated with a small but significant increased
48 consumption of antidepressants but a decreased incidence of psychiatric hospitalization. Suicide-
49 risk seemed increased in the second lockdown period.

50 Introduction

51 It has been suggested that the unprecedented mitigation policies imposed on the public during the
52 first and second wave of the Covid-19 pandemic could be associated with negative mental health
53 consequences [1–3].

54 At the time of the initial outbreak, no approved vaccines or curative treatments existed, thus the
55 containment of the pandemic relied on non-pharmaceutical measures, leading to nation-wide
56 implementations of social distancing measures. The severity of mitigation policies varied during the
57 pandemic with the periods March 12, 2020 – May 20, 2020 (lockdown period 1) and December 21,
58 2020 – March 1, 2021 (lockdown period 2), being the most heavily impacted. Measures imposed to
59 ensure social distancing included bans on private gatherings of more than 10 people and closing of
60 schools and liberal professions [4]. See Supplementary material, *Danish mitigation strategies*, for a
61 comprehensive overview of Danish mitigation strategies during SARS-CoV-2.

62 Prolonged periods of social distancing can cause isolation, where social connections and
63 interactions are absent or severely hampered [5]. Social isolation can, depending on individual
64 differences, lead to loneliness, an independent, but often co-occurring construct. Loneliness is a
65 subjective feeling of distress which can occur when social interactions are perceived as inadequate.
66 The individual perception of decreased social interaction thus facilitates the link between loneliness
67 and social isolation [5]. Loneliness is associated with suicidal ideation and symptoms related to
68 mental health [6,7]. Several studies have suggested that the Covid-19 pandemic, and the subsequent
69 changes in social interactions, have impacted the mental health status of the general population
70 [2,3].

71 Social distancing measures have served as pivotal tools in pandemic control and proved effective in
72 stemming the transmission of disease during the Covid-19 pandemic [8]. With the potential of

73 future pandemics, like Covid-19, it is likely that implementation of social distancing yet again will
74 become an important tool for disease mitigation, thus it is imperative to gain a better understanding
75 of the related mental health effects [9–11].

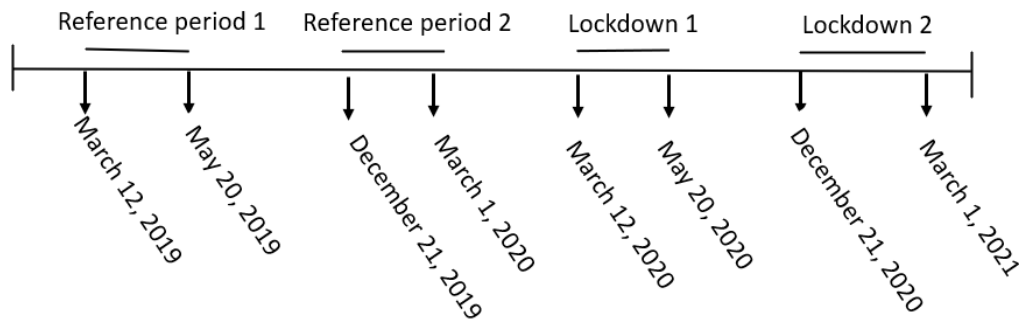
76 This nationwide cohort study involving the adult population of Denmark, investigated the potential
77 impact of severe social distancing measures on mental health outcomes. Specifically, we aimed to
78 assess whether these measures were associated with mental health disorders as assessed by
79 prescription of antidepressants, psychiatric hospitalization, and cases of suicide or suicide attempt.
80 We hypothesized that social distancing was associated with increased risk of collection of
81 prescriptions of antidepressants, admission to a psychiatric hospital department, and suicide
82 including suicide attempt in Denmark.

83 **Methods**

84 This is a nationwide retrospective population-based study utilizing the National Danish registries.
85 The study was approved by the Danish Data Protection Agency (j.no. P-2021-360). Informed
86 consent for retrospective studies is not required in Denmark. All Danish citizens are linked to a
87 unique identification number in the Civil Registration System [12], which in this study was used for
88 exact linkage at an individual level between registers, ensuring complete follow-up.

89 **Exposure periods**

90 There were two lockdown periods, and thus exposure periods, during the pandemic in Denmark:
91 March 12, 2020 – May 20, 2020 (lockdown period 1) and December 21, 2020 – March 1, 2021
92 (lockdown period 2) with corresponding reference periods: March 12, 2019 – May 20, 2019
93 (reference period 1) and December 21, 2019 – March 1, 2020 (reference period 2) (figure 1)



94

95 *Figure 1: definition of study periods*

96

97 **Data sources**

- 98
- 99 • The Danish Civil Registration System (CRS) includes individual information on the unique personal identification number, name, sex, date of birth and vital status [12].
 - 100 • The Danish National Patient Registry (DNPR) holds information on all admissions to Danish hospitals since 1977 and hospital outpatient clinic visits since 1995. Each hospital visit is coded by physicians with one primary diagnosis and one or more secondary diagnoses, according to the International Classification of Diseases, eighth revision (ICD8) codes until 1994 and ICD-10 thereafter[13]
 - 105 • The Danish National Health Service Prescription Database (DNHSPD) holds information on all prescriptions that have been dispensed in Danish pharmacies, since 2004 (coded according to the ATC classification system), including the following information in terms of OCS: the date of dispensation, the quantity dispensed as well as the strength and formulation of all prescriptions that have been dispensed from Danish Pharmacies. All pharmacies are required by Danish legislation to provide information that ensures complete and accurate registration[14]
 - 112 • The Cause of Death Register (DAR) holds information on all registered causes of deaths of Danish citizens since 1970 [15]
- 113

- 114 • The Danish Microbiology Database containing data on PCR-confirmed SARS-CoV-2
115 infection since February 2020[16]

116 Study population

117 The study population included all Danish adults (≥ 18 years) residing in Denmark (not including
118 Greenland and Faroe Islands) as of January 1st, 2019, and throughout the study period until March
119 1st, 2021. No exclusion criteria were applied. Individuals were censored in case of death or SARS-
120 CoV-2 infection. The latter was based on SARS-CoV-2 PCR-tests collected from nationwide
121 microbiological laboratories.

122 Outcomes

123 All outcomes were quantified during lockdown periods 1 and 2 as well as during reference periods
124 1 and 2 as described in ‘exposure periods’.

125 The primary outcome was collection of a prescription for antidepressants (Anatomical Therapeutic
126 Chemical classification codes, ATC, N06A including all sub-groups). Antidepressant prescription
127 collection was considered a binary variable with two possible outcomes, either none or at least one
128 prescription.

129 The two secondary outcomes were 1) admissions to a psychiatric ward, and 2) suicide and or
130 suicide attempt. A psychiatric admission was defined as any psychiatric ward contact lasting a
131 minimum of 24 hours, with a primary diagnosis of either depression (ICD-10: DF32, DF33, DF34),
132 anxiety (ICD-10: DF40-42, DF48, DF50) or bipolar disorder (ICD-10 codes DF30-31), including
133 maniac episodes (ICD-10: DF30).

134 Suicide was defined as ‘dead’ in the Civil Registration System and cause of death in the Cause of
135 Death Register, as serious self-harm or poisoning from mild pain relievers, including paracetamol
136 (ICD-10 DT39). Suicide attempt was defined as a hospital contact registered with primary diagnosis

137 of serious self-harm or poisoning from mild pain relievers, including paracetamol (ICD-10 DT39)
138 respectively.

139 A post-hoc sensitivity analysis was performed on suicide data across a combined exposure period
140 (lockdown period 1 and lockdown period 2) due to low amounts of suicide and suicide attempts
141 observed in the main analysis.

142 Additional post-hoc subanalyses were made on all endpoints stratifying for age and gender, *see*
143 *Supplementary Figure 3-5*. Antidepressant consumption was also stratified into groups of de novo
144 prescriptions (no prior prescription of antidepressants within 12 months of the particular period,
145 lockdown or reference) and non-de novo prescriptions (at least 1 prescription of any antidepressant
146 within 12 months of the particular period, lockdown or reference), *see supplementary table 1*.

147 Similarly, the endpoint regarding psychiatric hospitalization was stratified for de novo admissions
148 and readmissions (at least 1 psychiatric admission of minimum 24 hours within 12 months of the
149 particular period, lockdown or reference), *see Supplementary table 1*.

150 To investigate stockpiling of drugs at patients' homes and the potential impact on the collection of
151 antidepressant prescriptions, an analysis of the usage of enalapril, as control drug, was conducted.
152 Enalapril is widely used to treat chronic conditions such as hypertension and heart failure, thus, the
153 pandemic is not expected to have any major immediate impacts on its consumption, therefore
154 making it an ideal control drug for investigating stockpiling, *see supplementary table 2*.

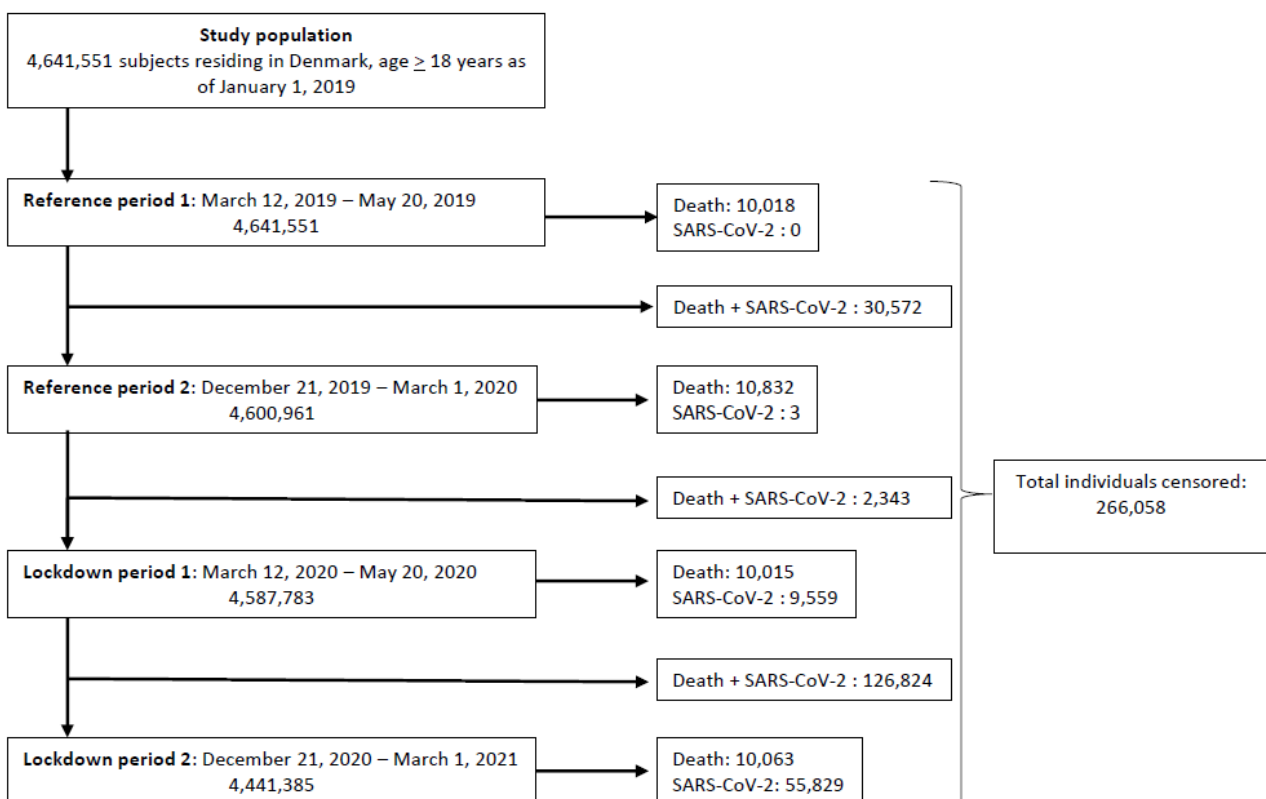
155 Statistical analysis

156 Categorical variables were presented as frequencies and absolute numbers. Continuous variables
157 were presented as means with 95% confidence intervals, or median values with interquartile ranges
158 (IQRs) depending on the data distribution. Primary and secondary outcomes were presented as
159 incidence rates (IR) and incidence rate ratios (IRR) with corresponding 95% confidence intervals

160 were calculated and compared using two-sided t-statistics. R software was used for statistical
 161 analysis.

162 Results

163 We identified a total of 4,641,551 individuals aged > 18 years (Figure 2). Baseline demographics
 164 and clinical characteristics are summarized in Table 1. Of these individuals, 595,175 (12,8%) had
 165 received at least one prescription of psychoactive medication and 231,847 (5,0%) suffered from a
 166 specialist treated psychiatric illness. As seen in Table 1, the baseline demographics remain similar
 167 during all four periods, with a slight decrease in median age and comorbidity score, this is primarily
 168 due to individuals censored for death being older and having more comorbidities than the average
 169 population, thus slightly altering the demographics during the study period. The censoring for death
 170 was consistent throughout all four periods, varying from 10,015 to 10,832 deaths per period.



171

172 *Figure 2: Study flowchart. All adults (≤ 18 years) residing in Denmark were included. No exclusion criteria were defined. Subjects*
 173 *were censored due to Death or SARS-CoV-2 infection.*

Table 1: Baseline patient demographic and clinical characteristics in a population of adult Danish citizens ≥ 18 years by 1 January 2019.

Characteristics	<i>Period 1</i>		<i>Period 2</i>	
	Reference Period (N = 4,641,551)	Lockdown Period (N = 4,587,783)	Reference Period (N = 4,600,961)	Lockdown Period (N = 4,441,385)
Age, median (IQR)	49 (33 to 64)	48 (33 to 64)	49 (33 to 64)	48 (33 to 63)
Male sex, n (%)	2,287,750 (49.29)	2,260,230 (49.27)	2,267,067 (49.27)	2,188,263 (49.27)
Medication				
Any psychoactive medication, n (%)	595,175 (12.82)	574,085 (12.51)	578,776 (12.58)	549,644 (12.38)
<i>Antidepressants</i>	393,051 (8.47)	379,593 (8.27)	382,618 (8.32)	363,477 (8.18)
<i>BZD and BZD-like</i>	244,572 (5.27)	233,651 (5.09)	236,046 (5.13)	222,686 (5.01)
<i>Antipsychotics</i>	113,364 (2.44)	108,868 (2.37)	109,803 (2.39)	104,232 (2.35)
<i>Lithium</i>	8733 (0.19)	8,564 (0.19)	8,605 (0.19)	8,269 (0.19)
Comorbidities				
Specialist treated psychiatric illness, n (%)	231,847 (5.00)	227,353 (4.96)	228,359 (4.96)	219,555 (4.94)
<i>Depression</i>	85475 (1.84)	82,959 (1.81)	83,502 (1.81)	79,470 (1.39)
<i>Anxiety disorders</i>	64,706 (1.39)	63,762 (1.39)	63,988 (1.39)	61,812 (1.39)
<i>Schizophrenia</i>	26,510 (0.57)	26,052 (0.57)	26,159 (0.57)	25,389 (0.57)
<i>Bipolar</i>	15,266 (0.33)	14,946 (0.33)	15,019 (0.33)	14,434 (0.32)

COPD, n (%)	144,288 (3.11)	136,234 (2.97)	138,058 (3.00)	127,844 (2.88)
Diabetes Mellitus, n (%)	138,467 (2.98)	131,607 (2.87)	133,115 (2.89)	123,997 (2.79)
Stroke and transient cerebral ischemia, n (%)	87,699 (1.89)	82,235 (1.79)	83,448 (1.81)	77,227 (1.74)
Charlson Comorbidity Index, mean (CI)	1.14 (1.14 to 1.14)	1.11 (1.11 to 1.11)	1.12 (1.12 to 1.12)	1.10 (1.09 to 1.10)

Abbreviations: IQR, Interquartile Range; COPD, Chronic Obstructive Lung Disease; CI, 95% Confidence Interval; BZD, benzodiazepine.

*Lock down period 1: March 12, 2020 – May 20, 2020 (reference period 1: March 12, 2019 – May 20, 2019)

** Lock down period 2: December 21, 2020 – March 1, 2021 (reference period 2: December 21, 2019 – March 1, 2020)

174 The incidence rates of collection of antidepressant prescriptions during reference period 1 and
175 lockdown period 1 were 564 per 100,000 person-weeks and 574 per 100,000 person-weeks
176 respectively. During reference period 2 and lockdown period 2, the IR was 552 per 100,000 person-
177 weeks and 598 per 100,000 person-weeks respectively, see table 2. This corresponds to an IRR of
178 1.02 (95% CI 1.01; 1.02, $p < 0.001$) for lockdown period 1 and 1.08 (95% CI 1.08; 1.09, $p < 0.001$)
179 for lockdown period 2. Cumulative incidences of collections of antidepressant prescriptions are
180 illustrated in Supplementary figure 1 and 2.

181 The incidence rates of psychiatric hospitalization during reference period 1 and lockdown period 1
182 were 36.9 per 100,000 person-weeks and 23.9 per 100,000 person-weeks respectively. During
183 reference period 2 and lockdown period 2 the IR was 35,9 per 100,000 and 30,9 per 100,000
184 respectively. This corresponds to an IRR of 0,65 (95% CI 0,63; 0,66, $p < 0.001$) for lockdown
185 period 1 and 0,86 (95% CI 0,84; 0,88 $p < 0.001$) for lockdown period 2 (Table 2). Thus, social
186 distancing was associated with a significantly decreased risk of psychiatric hospitalization during
187 both lockdown periods, particularly during the first period.

188 For suicide and suicide attempt, no statistically significant difference was found between reference
189 period 1 and lockdown period 1. However, during the second period of lockdown the IR was found
190 to increase from 0.69 per 100,000 during reference period 2 to 0.82 per 100,000 during lockdown
191 period 2, corresponding to an IRR of 1.19 (95% CI 1.02 ; 1.38 $p < 0,03$) (Table 2).

192
193

Table 2: Weekly incidences of psychiatric outcomes in periods with implemented COVID-19 lockdown measures compared to reference periods (same dates one year before) in a population of adult Danish citizens ≥ 18 years.

Persons/Subjects were censored when dead or PCR confirmed SARS-CoV-2 infection.

Outcomes	Period 1 *		Period 2 **	
	Reference Period (N = 4,641,551)	Lockdown Period (N = 4,587,783)	Reference Period (N = 4,600,961)	Lockdown Period (N = 4,441,385)
Antidepressants				
IR	564 per 100,000	574 per 100,000	552 per 100,000	598 per 100,000
IRR (95% CI)	Ref.	1.02 (1.01 to 1.02) $p < 0.001$	Ref.	1.08 (1.08 to 1.09) $p < 0.001$
Psychiatric hospital admission				
IR	36.96 per 100,000	23.85 per 100,000	35.93 per 100,000	30.90 per 100,000
IRR (95% CI)	Ref.	0.65 (0.63 to 0.66) $p < 0.001$	Ref.	0.86 (0.84 to 0.88) $p < 0.001$
Suicide and suicide attempt				
IR	0.64 per 100,000	0.62 per 100,000	0.69 per 100,000	0.82 per 100,000
IRR (95% CI)	Ref.	0.96 (0.82 to 1.13) $p = 0.64$	Ref.	1.19 (1.02 to 1.38) $p = 0.03$

Abbreviations: IR, Incidence Rate; IRR, Incidence Rate Ratio; CI, Confidence Interval.

*Lock down period 1: March 12, 2020 – May 20, 2020 (reference period 1: March 12, 2019 – May 20, 2019)

** Lock down period 2: December 21, 2020 – March 1, 2021 (reference period 2: December 21, 2019 – March 1, 2020)

194

195

196 Post-hoc subanalyses

197 From subanalyses stratifying for both age and gender, we saw that the biggest rise in antidepressant

198 consumption for the youngest age group, (18 – 32 years), with an IRR of 1.11 (95% CI 1.09 ; 1.14)

199 for women, and 1.09 (95% CI 1.06 ; 1.12) for men during lockdown period 1, and with similar

200 trends in lockdown 2, IRR 1.23 (95% CI 1.21 ; 1.25) for women, and 1.18 (95% CI 1.15 ; 1.21) for
201 men, *Supplementary figure 3*.

202 For psychiatric hospital admissions the impact of the lockdown periods were most apparent
203 amongst the elderly, age > 63 years, IRR 0,51 (95% CI 0.47 ; 0.56) for women, and 0.60 (95% CI
204 0.53 ; 0.68) for men during lockdown period 1 compared to 0.72 (95% CI 0.66 ; 0.78) for women,
205 and 0.81 (95% CI 0.73 ; 0.91) for men during lockdown period 2, *Supplementary figure 4*

206 For suicide and suicide attempts, no significant results were found during lockdown 1 when
207 stratifying for age and gender. However, during lockdown period 2, the IRR was increased for men
208 above 63 years 3.04 (95% CI 1.72 ; 5.38) as well as for women above 63 years 1.63 (95% CI 1.02 ;
209 2.60), *Supplementary figure 5*.

210 During lockdown period 1 there was an increased rate of antidepressant prescriptions with current
211 users were as the rate decreased for de novo prescriptions. For lockdown period 2 we saw increases
212 within both groups, with the biggest increase in de novo prescriptions, *Supplementary table 1*.

213 For psychiatric hospitalizations, the decrease was most pronounced for those that had a previous
214 hospitalization within 12 months compared to the group with no previous psychiatric admission
215 within 12 months, *Supplementary table 1*.

216 No increase in the consumption of “control drug” (Enalapril) was seen during either lockdown
217 period 1, *Supplementary table 2*.

218 The post-hoc sensitivity analysis on combined suicide and suicide attempts showed no significant
219 change in events from combined reference (IR 0.66) to combined exposure periods (IR 0.71), IRR
220 1,07 (95% CI 0.96; 1,20 p = 0,20).

221 Discussion

222 In this nationwide registry-based cohort study of 4,6 million Danish inhabitants, with a follow-up
223 time of 3.4 million person-years for the primary outcome, we found that the periods of social
224 distancing implemented to mitigate the SARS-CoV-2 pandemic, were associated with an increase in
225 collected prescriptions of antidepressant medication along with a significantly lower admission rate
226 to psychiatric wards compared to the pre pandemic reference periods. No significant difference was
227 detected in rates of suicide and suicide attempts during the initial lockdown period or in the post-
228 hoc combined exposure analysis. However, suicide-risk seemed increased in the second lockdown
229 period. Post-hoc subanalyses showed that the increase was most pronounced amongst the elderly.
230 It's important to interpret the findings regarding suicide cautiously, considering the limited
231 statistical power. Correspondingly, a systematic review of pre- and peri-pandemic suicide data
232 across 13 databases, found a nonsignificant downward trend for suicide rates during the pandemic,
233 however the study found increasing trends for both suicidal ideation and suicide attempts during the
234 pandemic [3].

235 The prescription of antidepressants exhibited a more substantial rise during Lockdown period 2
236 compared to the increase observed in Lockdown period 1. This trend might be related fatigue
237 experienced by individuals due to prolonged impact of the pandemic [17]. Factors such as
238 prolonged social isolation, economic challenges, and general uncertainties about the future could
239 have potentiated the negative mental health effects of social distancing, potentially leading to the
240 increased antidepressant consumption during the later stages of the pandemic. An impact was seen
241 across all age groups and genders, however post-hoc subanalyses show that results were most
242 pronounced amongst younger individuals between 18 and 32 years of age. This age distribution
243 corresponds well to other studies on mental health during Covid-19 [18]. Current users of

244 antidepressants saw similar increases during both lockdown periods, whereas the number of new
245 users decreased during the first lockdown but increased during the second.

246 A Swedish study of 1.4 million inhabitants in the region of Scania found no changes in the trends of
247 common psychotropic medications after March 2020, concluding that the public mental health was
248 not affected by the Covid-19 pandemic in a way that altered the use of psychotropic medication.
249 The Swedish government strategies for mitigating the covid-19 pandemic differed from those
250 applied in Denmark and most other countries, relying primarily on recommendations rather than
251 restrictions, thus abstaining from full-scale lockdown [19]. As there are otherwise noteworthy
252 similarities between the two Scandinavian populations, the increased consumption of
253 antidepressants found in this current study, compared to that of the Swedish study, could be
254 attributed to the more extensive social distancing measures applied in Denmark compared to
255 Sweden. However, it is important to note that mobility data shows similar trends for cell phone
256 mobility data from April 2020 and onward when comparing Sweden and other Nordic countries,
257 including Denmark [20]. This suggests that differences in real world pandemic mitigation strategies
258 are more subtle than otherwise indicated by steps taken at a national level.

259 An analysis conducted by the Danish Health Data Authority concludes that the Danish consumption
260 of antidepressants in 2020 has been stable in relation to the last five years, however, similar to the
261 findings of this current study, they found increased consumption in March 2020 and December
262 2020, corresponding to the initiation of the first and second national lockdown periods [21].

263 No increases in enalapril usage were seen during either lockdown periods and thus there is no clear
264 evidence of stockpiling occurring and subsequently affecting the findings of this study.

265 The increased consumption of antidepressants contrasts the decreased psychiatric hospitalization
266 rate. This could, however, be attributed to an elevated threshold for health care contact during the

267 pandemic, rather than a lower prevalence of psychiatric disorders requiring hospitalization. Somatic
268 diseases, such as cardiovascular disorders saw similarly lower incidences in Denmark during the
269 covid-19 pandemic [22,23]. The studies in question suggest that lower admission rates are, in part,
270 caused by a crisis driven threshold-raise for, patients contacting a physician when experiencing
271 symptoms, and the physician agreeing to a consultation. Similar mechanisms can explain the
272 decreased psychiatric hospitalization rate, potentially unveiling a temporary underdiagnosis of
273 psychiatric (as well as somatic) disorders, with issues related to untreated mental illness presenting
274 themselves at a later stage.

275 The increased consumption of antidepressants could, in part, be explained by a shift from inpatient
276 care to outpatient care, highlighted by the decreased rate of psychiatric hospitalization. During
277 lockdown period 2 however, the absolute increase in the number of people collecting a prescription
278 for antidepressants greatly exceeds the corresponding decrease in psychiatric hospitalization. The
279 decrease in inpatient care can therefore only explain a small part of the increased consumption of
280 antidepressants.

281 A major strength of this study is that we followed the entire adult Danish population, allowing for a
282 sample size of 4.6 million Danish inhabitants, providing extensive statistical power. The inclusion
283 of essentially all Danish adult residents in the cohort allows generalizability to national populations
284 compared to other studies based on smaller, selected databases which may not be representative of
285 the general population. Secondly, this study was able to compare virtually the same population with
286 itself at different points in time, with subtle differences in the actual populations, thereby limiting
287 the effects of possible confounders to some extent.

288 Thirdly, due to the extensiveness of the Danish registries on health data, no subjects were lost to
289 follow-up. We had access to complete and validated data on prescriptions, hospital admissions and
290 causes of death.

291 Furthermore, the censoring of SARS-CoV-2 infected individuals was based on a PCR validated
292 SARS-CoV-2 diagnosis via real-time nationwide microbiological data from central laboratories, no
293 self-tests. Covid-19 infection has been linked to an increased use of psychoactive medication [24]
294 and could contribute to an increased signal, unrelated to the social distancing measures, thus SARS-
295 CoV-2 infected individuals were censored. This does however also introduce a slight risk of bias, as
296 those infected with Covid-19 differ from the total population as they are generally younger, less
297 medicated with psychoactive medication and have fewer comorbidities [24]. However, this
298 amounts to less than 200,000 individuals censored due to SARS-CoV-2 infection, out of a total
299 sample size of 4.6 million and is therefore not expected to drive a signal.

300 There are some limitations to this study. Firstly, this study holds no information on adherence to
301 social distancing guidelines and thus solely relies on the governmental implementations. A lack of
302 adherence would tend to weaken our signal.

303 It has been shown from survey data, that living alone during Covid-19 was associated with higher
304 levels of loneliness and lower life satisfaction [25]. This study does not have access to data on type
305 of residence and dwelling, this would otherwise have added valuable information on whether
306 specific living alone, or other living situations, would impact the endpoints investigated in this
307 study.

308 The analyses of this study were based on observations before and after the intervention of social
309 distancing, thus the follow-up was limited to the exposure time. The findings of this study would be
310 further strengthened, by observing an expected normalization of both antidepressant consumption

311 and psychiatric hospitalization in the corresponding time periods following the removal of social
312 distancing measures. Collection of antidepressant medications does not necessarily reflect the
313 mental health status of the population, as filed prescriptions are also influenced by several other
314 factors. Other psychoactive medications can too be used to reflect the mental health status of a
315 population. However, depression and anxiety disorders account for more than half the specialist
316 treated psychiatric illnesses within the study population. For both conditions, antidepressants are
317 often first-line pharmacological treatment. In the current study, antidepressants account for two
318 thirds of the total use of psychoactive medication in the population. Furthermore, due to frequent
319 reports of symptoms related to anxiety and affective disorders during the Covid-19 pandemic, it is
320 hypothesized that these conditions are the psychiatric disorders most likely to be influenced by the
321 lockdown periods [26]. Therefore, we believe that the consumption rate of antidepressant
322 medication is a reliable indicator of public mental health status during the Covid-19 lockdowns but
323 recognize that it does not provide a complete picture.

324 The impacts of the lockdowns are complex, and several factors are likely to have influenced the
325 mental health of the general public during the pandemic, these include anxiety towards the future,
326 job and economic uncertainties, governmental distrust, fear of dying or losing loved ones. It has
327 also been hypothesized, that the lockdowns periods have had positive impacts, such as increased
328 time spend with family and being outdoors, along with a deceleration of the societal rhythm.

329 With data based on a nationwide cohort, this study aimed to provide valid and generalizable results
330 without non-response induced bias. To our knowledge this study is currently the largest study of
331 nationwide data on consumption of antidepressant medication, psychiatric hospitalization and
332 suicide and suicide attempt.

333 In conclusion, in this nationwide cohort study of the entire 4,6 million adult population of Denmark,
334 we found an increase in the consumption of antidepressant medication, in particular amongst young
335 adults during two separate periods of social distancing during the Covid-19 pandemic. Concurrently
336 we saw a significantly decreased rate of psychiatric hospitalization. Rates of suicide and suicide
337 attempts increased during the second lockdown period, especially amongst the elderly.

338 The results of this study should contribute to the debate over an increased monitoring of possible
339 residual damage to public mental health following the Covid-19 pandemic. Simultaneously, this
340 study brings valuable insights about the possible effects of social distancing, which can and should
341 be taken into consideration by governments and health care authorities in the event of a future
342 pandemic demanding a social distancing-based mitigation strategy.

343

344 **Acknowledgement**

345 We thank the COP:TRIN (coptrin.dk) Steering Committee and the CURE group (copresp.dk) for
346 their valuable contributions to this study during meetings

347 **Conflict of interest statement**

348 None of the authors have any conflicts of interest.

349 **Funding sources**

350 NNF COVID-19 grant NNF20SA0062834

351 **Author contributions**

352 Andreas Geest (*Corresponding author*), Barbara Bonnesen (*Data curation, writing – review &*
353 *editing: supporting*), Alexander Jordan (*Formal analysis: Supporting, writing – review & editing:*
354 *Supporting*), Louise Tønnesen (*Data curation: Supporting, Writing – review & editing: Supporting*)
355 Valdemar Rømer (*Formal analysis: Supporting, Software: Supporting, Visualization: Equal,*
356 *Writing – review & editing: Supporting*) Charlotte s. Ulrik (*Methodology: Supporting, Writing –*
357 *review & editing: Supporting*), Zitta b. Harboe (*Methodology: Supporting, Writing – review &*
358 *editing: Supporting*), Josefin Eklöf (*Conceptualization: Supporting, Formal analysis: Supporting,*
359 *Methodology: Supporting, Supervision: Supporting, Writing – review & editing: Supporting*),
360 Pradeesh Sivapalan (*Conceptualization: Supporting, Formal analysis: Supporting, Supervision:*
361 *Supporting, Writing – review & editing: Supporting*), Jens-Ulrik Stæhr Jensen (*Conceptualization:*
362 *Supporting, Formal analysis: Supporting, Methodology: Supporting, Supervision: Supporting,*
363 *Writing – review & editing: Supporting*)

364 **Data sharing statement**

365 We believe that knowledge sharing increases the quantity and quality of scientific results. Sharing
366 of relevant data will be discussed within the study group upon reasonable request. All data sharing
367 should respect Danish legislation

368

369

370 **References**

- 371 [1] Liu CH, Zhang E, Wong GTF, Hyun S, Hahm H “Chris.” Factors associated with depression, anxiety,
372 and PTSD symptomatology during the COVID-19 pandemic: Clinical implications for U.S. young adult
373 mental health. *Psychiatry Res* 2020;290:113172. <https://doi.org/10.1016/j.psychres.2020.113172>.
- 374 [2] Ahmed N, Barnett P, Greenburgh A, Pemovska T, Stefanidou T, Lyons N, et al. Mental health in
375 Europe during the COVID-19 pandemic: a systematic review. *Lancet Psychiatry* 2023;10:537–56.
376 [https://doi.org/10.1016/S2215-0366\(23\)00113-X](https://doi.org/10.1016/S2215-0366(23)00113-X).
- 377 [3] Yan Y, Hou J, Li Q, Yu NX. Suicide before and during the COVID-19 Pandemic: A Systematic Review
378 with Meta-Analysis. *Int J Environ Res Public Health* 2023;20:3346.
379 <https://doi.org/10.3390/ijerph20043346>.
- 380 [4] SSI oversigt og tidslinje over Covid-19 i Danmark og udland
381 <https://www.ssi.dk/aktuelt/nyheder/2022/da-covid-19-ramte-verden-og-danmark-se-tidslinjen-her>
382 n.d.
- 383 [5] Matthews T, Danese A, Wertz J, Odgers CL, Ambler A, Moffitt TE, et al. Social isolation, loneliness
384 and depression in young adulthood: a behavioural genetic analysis. *Soc Psychiatry Psychiatr*
385 *Epidemiol* 2016;51:339–48. <https://doi.org/10.1007/s00127-016-1178-7>.
- 386 [6] Matthews T, Danese A, Wertz J, Odgers CL, Ambler A, Moffitt TE, et al. Social isolation, loneliness
387 and depression in young adulthood: a behavioural genetic analysis. *Soc Psychiatry Psychiatr*
388 *Epidemiol* 2016;51:339–48. <https://doi.org/10.1007/s00127-016-1178-7>.
- 389 [7] Beutel ME, Klein EM, Brähler E, Reiner I, Jünger C, Michal M, et al. Loneliness in the general
390 population: prevalence, determinants and relations to mental health. *BMC Psychiatry* 2017;17:97.
391 <https://doi.org/10.1186/s12888-017-1262-x>.
- 392 [8] Chu DK, Akl EA, Duda S, Solo K, Yaacoub S, Schünemann HJ, et al. Physical distancing, face masks,
393 and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a
394 systematic review and meta-analysis. *The Lancet* 2020;395:1973–87.
395 [https://doi.org/10.1016/S0140-6736\(20\)31142-9](https://doi.org/10.1016/S0140-6736(20)31142-9).
- 396 [9] Morens DM, Fauci AS. Emerging Pandemic Diseases: How We Got to COVID-19. *Cell* 2020;182:1077–
397 92. <https://doi.org/10.1016/j.cell.2020.08.021>.

- 398 [10] Morens DM, Taubenberger JK. Pandemic influenza: certain uncertainties. *Rev Med Virol* 2011;n/a-
399 n/a. <https://doi.org/10.1002/rmv.689>.
- 400 [11] Morse SS, Mazet JA, Woolhouse M, Parrish CR, Carroll D, Karesh WB, et al. Prediction and
401 prevention of the next pandemic zoonosis. *The Lancet* 2012;380:1956–65.
402 [https://doi.org/10.1016/S0140-6736\(12\)61684-5](https://doi.org/10.1016/S0140-6736(12)61684-5).
- 403 [12] Pedersen CB. The Danish Civil Registration System. *Scand J Public Health* 2011;39:22–5.
404 <https://doi.org/10.1177/1403494810387965>.
- 405 [13] Schmidt M, Schmidt SAJ, Sandegaard JL, Ehrenstein V, Pedersen L, Sørensen HT. The Danish National
406 Patient Registry: a review of content, data quality, and research potential. *Clin Epidemiol* 2015:449.
407 <https://doi.org/10.2147/CLEP.S91125>.
- 408 [14] Johannesdottir SA, Horváth-Puhó E, Ehrenstein V, Schmidt, Pedersen L, Sørensen H. Existing data
409 sources for clinical epidemiology: The Danish National Database of Reimbursed Prescriptions. *Clin*
410 *Epidemiol* 2012:303. <https://doi.org/10.2147/CLEP.S37587>.
- 411 [15] Helweg-Larsen K. The Danish Register of Causes of Death. *Scand J Public Health* 2011;39:26–9.
412 <https://doi.org/10.1177/1403494811399958>.
- 413 [16] Schønning K, Dessau RB, Jensen TG, Thorsen NM, Wiuff C, Nielsen L, et al. Electronic reporting of
414 diagnostic laboratory test results from all healthcare sectors is a cornerstone of national
415 preparedness and control of COVID-19 in Denmark. *APMIS* 2021;129:438–51.
416 <https://doi.org/10.1111/apm.13140>.
- 417 [17] Australian psychological society. Lockdown fatigue by Australian psychological society
418 [https://psychology.org.au/getmedia/74e7a437-997c-4eea-a49c-30726ce94cf0/20aps-is-covid-19-](https://psychology.org.au/getmedia/74e7a437-997c-4eea-a49c-30726ce94cf0/20aps-is-covid-19-public-lockdown-fatigue.pdf)
419 [public-lockdown-fatigue.pdf](https://psychology.org.au/getmedia/74e7a437-997c-4eea-a49c-30726ce94cf0/20aps-is-covid-19-public-lockdown-fatigue.pdf) n.d.
- 420 [18] Santomauro DF, Mantilla Herrera AM, Shadid J, Zheng P, Ashbaugh C, Pigott DM, et al. Global
421 prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020
422 due to the COVID-19 pandemic. *The Lancet* 2021;398:1700–12. [https://doi.org/10.1016/S0140-](https://doi.org/10.1016/S0140-6736(21)02143-7)
423 [6736\(21\)02143-7](https://doi.org/10.1016/S0140-6736(21)02143-7).
- 424 [19] Wolfschlag M, Grudet C, Håkansson A. Impact of the COVID-19 Pandemic on the General Mental
425 Health in Sweden: No Observed Changes in the Dispensed Amount of Common Psychotropic
426 Medications in the Region of Scania. *Front Psychiatry* 2021;12.
427 <https://doi.org/10.3389/fpsy.2021.731297>.
- 428 [20] Yarmol-Matusiak EA, Cipriano LE, Stranges S. A comparison of COVID-19 epidemiological indicators
429 in Sweden, Norway, Denmark, and Finland. *Scand J Public Health* 2021;49:69–78.
430 <https://doi.org/10.1177/1403494820980264>.
- 431 [21] Danskernes brug af antidepressiv medicin har været stabilt under COVID-19.
432 https://sundhedsdatastyrelsen.dk/da/nyheder/2021/antidepressiva2020_260321 2021.
- 433 [22] Andersson C, Gerds T, Fosbøl E, Phelps M, Andersen J, Lamberts M, et al. Incidence of New-Onset
434 and Worsening Heart Failure Before and After the COVID-19 Epidemic Lockdown in Denmark: A
435 Nationwide Cohort Study. *Circ Heart Fail* 2020;13:e007274.
436 <https://doi.org/10.1161/CIRCHEARTFAILURE.120.007274>.

- 437 [23] Holt A, Gislason GH, Schou M, Zareini B, Biering-Sørensen T, Phelps M, et al. New-onset atrial
438 fibrillation: incidence, characteristics, and related events following a national COVID-19 lockdown of
439 5.6 million people. *Eur Heart J* 2020;41:3072–9. <https://doi.org/10.1093/eurheartj/ehaa494>.
- 440 [24] Rømer V, Sivapalan P, Eklöf J, Nielsen SD, Harboe ZB, Biering-Sørensen T, et al. SARS-CoV-2 and risk
441 of psychiatric hospital admission and use of psychopharmaceuticals: A nationwide registry study of
442 4,585,083 adult Danish citizens. *European Psychiatry* 2023;66:e50.
443 <https://doi.org/10.1192/j.eurpsy.2023.2418>.
- 444 [25] Keller A, Groot J, Matta J, Bu F, El Aarbaoui T, Melchior M, et al. Housing environment and mental
445 health of Europeans during the COVID-19 pandemic: a cross-country comparison. *Sci Rep*
446 2022;12:5612. <https://doi.org/10.1038/s41598-022-09316-4>.
- 447 [26] Ferwana I, Varshney LR. The impact of COVID-19 lockdowns on mental health patient populations in
448 the United States. *Sci Rep* 2024;14:5689. <https://doi.org/10.1038/s41598-024-55879-9>.
- 449