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Research paper

# Contributions of specific causes of death by age to the shorter life expectancy in depression: a register-based observational study from Denmark, Finland, Sweden and Italy

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ABSTRACT

*Background:* The reasons for the shorter life expectancy of people with depression may vary by age. We quantified the contributions of specific causes of death by age to the life-expectancy gap in four European countries.
*Methods:* Using register-based cohort data, we calculated annual mortality rates in between 1993 and 2007 for psychiatric inpatients with depression identified from hospital-care registers in Denmark, Finland and Sweden, and between 2000 and 2007 for antidepressant-treated outpatients identified from medication registers in Finland and Turin, Italy. We decomposed the life-expectancy gap at age 15 years by age and cause of death.
*Results:* The life-expectancy gap was especially large for psychiatric inpatients (12.1 to 21.0 years) but substantial also for antidepressant-treated outpatients (6.3 to 14.2 years). Among psychiatric inpatients, the gap was largely attributable to unnatural deaths below age 55 years. The overall contribution was largest for suicide in Sweden (43 to 45%) and Finland (37 to 40%). In Denmark, 'other diseases' (25 to 34%) and alcohol-attributable causes (10 to 18%) had especially large contributions. Among antidepressant-treated outpatients, largest contributions were observed for suicide (18% for men) and circulatory deaths (23% for women) in Finland, and cancer deaths in Turin (29 to 36%). Natural deaths were concentrated at ages above 65 years.
*Limitations:* The indication of antidepressant prescription could not be ascertained from the medication registers.
*Conclusions:* Interventions should be directed to self-harm and substance use problems among younger psychiatric inpatients and antidepressant-treated young men. Rigorous monitoring and treatment of comorbid somatic conditions and disease risk factors may increase life expectancy for antidepressant-treated outpatients, especially women.

## 1. Introduction

People with depression live shorter lives than those without depression. The gap in life expectancy in depression or affective disorders has been estimated at around 7 to 17 years (Chang et al., 2011; Laursen et al., 2016; Nordentoft et al., 2013; Walker et al., 2015). People with depression experience elevated all-cause mortality rates and mortality due to several specific causes of death. Suicide mortality is known to be particularly high in depression, the risk of suicide being about 20 times higher than in the general population (Chesney et al., 2014; Harris and Barraclough, 1998). Several studies show, however, that natural causes of death account for the majority of premature deaths in

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depression (Lawrence et al., 2013; Swaraj et al., 2019; Walker et al., 2015; Wulsin et al., 1999).

A Danish register study found that mortality due to unnatural causes, including suicide and other external causes, for people with severe depression was particularly elevated at ages below 60 years compared to older age groups (Laursen et al., 2016). This follows the general age-pattern in the cause-of-death structure as suicide and other external causes rank among the leading causes of death at younger ages, while cardiovascular disease, cancer and respiratory diseases make up an increasing proportion of deaths with advancing age (Brooke et al., 2017; Peden et al., 2002). Based on the existing evidence, it is unclear how these cause-specific mortality rates contribute to the lower life expectancy of people with depression. On the one hand, deaths at younger ages, such as suicides, contribute more to life years lost and thus have a greater impact on life expectancy than deaths at older ages. On the other hand, disease deaths at older ages may have a greater impact due to their greater incidence. To the best of our knowledge, however, no previous study has quantified the age-specific contributions of different causes of death to the gap in life expectancy in depression. Quantifying these contributions will help in targeting preventive measures where they have the greatest population level impact.

To fill the gap in the literature, we quantified the contribution of excess mortality from specific causes of death at different ages to the gap in life expectancy in depression. We assessed these contributions separately for psychiatric inpatients treated for depression and antidepressant-treated outpatients, and in three Nordic and one Southern European country. We identified psychiatric inpatients from national hospital registers of Denmark, Finland and Sweden, and antidepressant-treated outpatients from medication registers of Finland and Turin, Italy. Comparison of different country contexts and patient groups gives a more comprehensive view to the range of the contribution of different causes of death to the life expectancy gap in depression.

## 2. Methods

### 2.1. Data

We employed population registers linked with administrative health care records in four different countries: Denmark, Finland, Sweden and Italy. For Denmark and Sweden, the data set included the total populations of the countries between 1993 and 2007, and for Italy, the total population of the city of Turin between 2000 and 2007 using data from the Turin Longitudinal Study. The data for Finland comprised an 11% random sample representative of the Finnish population between 1993 and 2007, supplemented with an 80% random sample of people who died in the period. The Finnish analyses were weighted to account for the differing sampling probabilities of people who died and who survived the period.

### 2.2. Mortality

Data on mortality was based on national death registers. We calculated annual deaths per person-years at risk between 1993 and 2007 and pooled the numbers across calendar years to obtain stable rates of cause-specific mortality. Deaths were calculated by 5-year age groups, sex and the underlying cause of death. We used eight broad categories of causes of death and identified them using the 8th, 9th and 10th revisions of International Classification of Diseases (ICD): lung cancer, other cancers, circulatory diseases, respiratory diseases, alcohol-attributable causes (including alcohol-attributable diseases and accidental poisoning by alcohol), all other diseases, suicide and all other external causes (i.e. accidents and violence). The specific ICD-codes for the causes of death are presented in Supplementary Tables S1 and S2.

### 2.3. Depression

To identify individuals with depression, we employed health registers available in each country: for Denmark, Finland and Sweden we used hospital inpatient care registers, and for Finland and Turin we used records of state-reimbursed medication purchases (Finland) and prescriptions (Turin). Hospital care episodes with a depression diagnosis were identified using ICD-8, ICD-9 and ICD-10 (for more detail see Supplementary Table S1). Anatomical Therapeutic Chemical (ATC) code N06A was used for identifying antidepressant purchases and prescriptions. A person was considered as depressed if they had a previous psychiatric inpatient care episode one to five years preceding (covering years from 1988 to2006) each one-year spell of mortality follow-up between 1993 and 2007 (“depressed psychiatric inpatients”), or had a purchase of or prescription for antidepressants one to three years preceding (covering years from 1997 to 2006) each spell of mortality follow-up between 2000 and 2007 (“antidepressant-treated outpatients”). Compared to psychiatric inpatient care, antidepressants may be prescribed for milder and more transient depressive episodes and therefore we restricted the time window of antidepressant purchases and prescriptions to fewer years. The mortality follow-up of antidepressant-treated outpatients was shorter due to the availability of medication data being limited to more recent years. The register data on medication did not include information on diagnosis, and thus some of those we identified as antidepressant-treated outpatients may not have been treated for depression. For further discussion, please see the section Strengths and limitations. Because data on both antidepressants and inpatient care was only available in the Finnish data, we did not consider whether the antidepressant-treated outpatients had also had a psychiatric inpatient care episode. To assess the extent to which this affected our results, we conducted a sensitivity analysis on the Finnish data where we considered only antidepressant-treated outpatients with no psychiatric inpatient care episodes within the past 5 years.

### 2.4. Life tables and decomposition

We calculated remaining life expectancy at age 15 years for men and women with and without depression in the four countries using the abridged life table method (Shyrock and Siegel, 1976). We decomposed the gap in life expectancy into contributions of specific 5-year age groups (results shown for 10-year age groups) and causes of death applying the method used by United Nations (United Nations, 1988; Ponnapalli, 2005). In short, the method first decomposes the difference in life expectancy into years contributed by each age group, and then decomposes the difference by cause of death within each age group based on age and cause-specific mortality rates. The formulae used for the decomposition are presented in Supplementary File Appendix A. Microsoft Excel was used for life table calculations and decomposition.

## 3. Results

The remaining life expectancy at age 15 years for people with depression was several years shorter than that for those without, using both definitions of depression. For psychiatric inpatients with depression, the male and female life expectancy gaps were 21.0 and 18.0 years, respectively, in Denmark, 19.9 and 15.4 years, respectively, in Finland, and 15.9 and 12.1 years, respectively, in Sweden (Table 1). For antidepressant-treated outpatients, the gap in life expectancy was smaller: the male and female life expectancy gaps were 14.2 and 8.0 years, respectively, in Finland, and 11.9 and 6.3 years, respectively, in Turin.

Table 2 shows the contributions of specific causes of death to the life-expectancy gap between those with and without depression. For psychiatric inpatient women and men suicide had the largest contribution to the life-expectancy gap in Sweden (7.1 years [45%] for men; 5.2 years [43%] for women) and in Finland (8.0 years [40%] for men; 5.8 years

**Table 1**
Person years, number of deaths, remaining life expectancy at age 15 years and the gap in life expectancy between individuals with and without depression by sex in Denmark, Finland, Sweden and Turin, Italy, 1993 2007.

| | | Depression | | | | No depression | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Depression prevalence[†] | Person years | Deaths | Remaining life expectancy at age 15 years | | Person years | Deaths | Remaining life expectancy at age 15 years | | Gap in life expectancy at age 15 years |
| Definition of depression | (%) | (1000s) | (1000s) | (years) | (95% CI) | (1000s) | (1000s) | (years) | (95% CI) | (years) |
| *Psychiatric inpatients with depression* | | | | | | | | | | |
| *Denmark* | | | | | | | | | | |
| Men | 0.2 | 50 | 5 | 38.6 | 37.1 to 40.0 | 30,565 | 420 | 59.5 | 59.4 to 59.5 | 21.0 |
| Women | 0.3 | 99 | 9 | 46.2 | 45.2 to 47.3 | 31,727 | 434 | 64.2 | 64.2 to 64.3 | 18.0 |
| *Finland* | | | | | | | | | | |
| Men | 0.7 | 46 | 2 | 39.5 | 38.0 to 41.1 | 6513 | 76 | 59.4 | 59.3 to 59.5 | 19.9 |
| Women | 0.9 | 64 | 2 | 50.9 | 49.7 to 52.2 | 6971 | 77 | 66.3 | 66.2 to 66.4 | 15.4 |
| *Sweden* | | | | | | | | | | |
| Men | 0.3 | 155 | 6 | 47.7 | 46.8 to 48.5 | 54,570 | 678 | 63.6 | 63.6 to 63.6 | 15.9 |
| Women | 0.5 | 268 | 8 | 56.0 | 55.4 to 56.6 | 56,393 | 697 | 68.1 | 68.1 to 68.2 | 12.1 |
| *Antidepressant-treated outpatients*[†] | | | | | | | | | | |
| *Finland* | | | | | | | | | | |
| Men | 7.1 | 256 | 8 | 47.3 | 46.6 to 48.1 | 3310 | 33 | 61.6 | 61.4 to 61.7 | 14.2 |
| Women | 11.9 | 452 | 11 | 60.1 | 59.6 to 60.5 | 3353 | 31 | 68.1 | 67.9 to 68.1 | 8.0 |
| *Turin* | | | | | | | | | | |
| Men | 5.5 | 165 | 7 | 51.2 | 49.6 to 52.8 | 2851 | 31 | 63.2 | 63.0 to 63.3 | 11.9 |
| Women | 10.8 | 362 | 9 | 62.7 | 61.9 to 63.5 | 2981 | 31 | 69.1 | 69.0 to 69.3 | 6.3 |

[†] Person years depressed as a proportion of total person years.
[‡] Mortality follow-up between 2000 and 2007.

**Table 2**
Decomposition of the gap in life expectancy at age 15 years by cause of death, men and women in Denmark, Finland, Sweden and Turin, Italy, in 1993 2007.

| *Psychiatric inpatients with depression* | Denmark | | | | Finland | | | | Sweden | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Men | | Women | | Men | | Women | | Men | | Women | |
| | Years | % | Years | % | Years | % | Years | % | Years | % | Years | % |
| Lung cancer | 0.4 | 2 | 0.7 | 4 | 0.2 | 1 | 0.2 | 1 | 0.1 | 1 | 0.2 | 2 |
| Other cancers | 1.2 | 6 | 1.7 | 9 | 0.3 | 1 | 0.4 | 3 | 0.5 | 3 | 0.8 | 6 |
| Circulatory diseases | 3.2 | 15 | 2.8 | 16 | 3.0 | 15 | 3.0 | 20 | 2.5 | 16 | 2.1 | 18 |
| Respiratory diseases | 1.3 | 6 | 2.0 | 11 | 1.0 | 5 | 0.8 | 5 | 0.7 | 4 | 0.8 | 6 |
| Alcohol-attributable causes | 3.8 | 18 | 1.8 | 10 | 2.3 | 12 | 1.1 | 7 | 0.6 | 4 | 0.1 | 1 |
| Other diseases | 5.2 | 25 | 6.1 | 34 | 1.6 | 8 | 2.2 | 14 | 2.3 | 15 | 1.6 | 14 |
| Suicide | 4.4 | 21 | 2.2 | 12 | 8.0 | 40 | 5.8 | 37 | 7.1 | 45 | 5.2 | 43 |
| Other external causes | 1.5 | 7 | 0.7 | 4 | 3.5 | 18 | 2.0 | 13 | 2.1 | 13 | 1.3 | 11 |
| Total | 21.0 | 100 | 18.0 | 100 | 19.9 | 100 | 15.4 | 100 | 15.9 | 100 | 12.1 | 100 |

| *Antidepressant-treated outpatients*[†] | Finland | | | | Turin | | | |
|---|---|---|---|---|---|---|---|---|
| | Men | | Women | | Men | | Women | |
| | Years | % | Years | % | Years | % | Years | % |
| Lung cancer | 0.3 | 2 | 0.2 | 3 | 0.9 | 8 | 0.3 | 4 |
| Other cancers | 1.1 | 8 | 1.3 | 16 | 2.5 | 21 | 2.0 | 32 |
| Circulatory diseases | 2.6 | 18 | 1.8 | 23 | 1.5 | 13 | 1.0 | 16 |
| Respiratory diseases | 0.7 | 5 | 0.4 | 5 | 0.7 | 6 | 0.3 | 5 |
| Alcohol-attributable causes | 2.0 | 14 | 0.6 | 7 | 0.1 | 1 | 0.0 | 1 |
| Other diseases | 1.8 | 12 | 1.5 | 18 | 4.5 | 38 | 2.0 | 31 |
| Suicide | 3.2 | 23 | 1.4 | 17 | 1.4 | 12 | 0.6 | 9 |
| Other external causes | 2.6 | 18 | 0.8 | 10 | 0.3 | 2 | 0.1 | 2 |
| Total | 14.2 | 100 | 8.0 | 100 | 11.9 | 100 | 6.3 | 100 |

Percentages may not add up to 100 due to rounding.
[†] Mortality follow-up between 2000 and 2007.

[37%] for women). Suicide also had a substantial contribution to the gap among Danish men (4.4 years; 21%). Alcohol-attributable causes had a particularly large contribution for men in Denmark (3.8 years; 18%) and Finland (2.3 years; 12%), as did other external causes in Finland (3.5 years; 18%). Of the somatic diseases, circulatory diseases consistently contributed to the gap by 2 to 3 years in all three countries. In contrast to Finland and Sweden, 'other diseases' had a substantial contribution to the life-expectancy gap in Denmark (5.2 years [25%] for men; 6.1 years [34%] for women).

For antidepressant-treated outpatients, the largest contributions to the life-expectancy gap were by circulatory diseases in Finland and cancers in Turin. Circulatory diseases accounted for 2.6 years (18%) and 1.8 years (23%) of the gap for Finnish men and women, respectively, and cancers for 3.4 years (29%) and 2.3 years (36%) for Turinese men and women, respectively. In Turin, 'other diseases' also had a large contribution to the life-expectancy gap (4.5 years [38%] for men; 2.0 years [31%] for women). For Finnish outpatient men, large contributions were observed for suicide (3.2 years; 23%), other external causes (2.6 years; 18%) and alcohol-attributable causes of death (2.0 years; 14%).

The gap in life expectancy for psychiatric inpatients was largely attributable to deaths between ages 25 and 54 years, especially among men (Fig. 1). The large contribution of these age groups was primarily due to suicide and other external causes of death. The marked contribution of alcohol-attributable causes of death in Denmark and Finland was also due to deaths below age 55 years. For antidepressant-treated outpatients, the life-expectancy gap was predominantly attributable to somatic diseases at older ages (Fig. 2). The largest contributions were observed for circulatory deaths above age 65 years for Finnish women (1.4 years) and cancer deaths above age 45 years for Turinese men (2.5 years) and women (1.7 years). For men, deaths at ages 15 to 24 years had a particularly large contribution in both Finland (2.4 years) and Turin (2.8 years), these deaths being largely attributable to suicide and other external causes in Finland, and "other diseases" and suicide in Turin. The exact values for age-specific contributions of each cause of death are presented in Supplementary Tables S3 and S4.

To assess the extent to which our results on antidepressant-treated outpatients were driven by the fact that some may have also had more

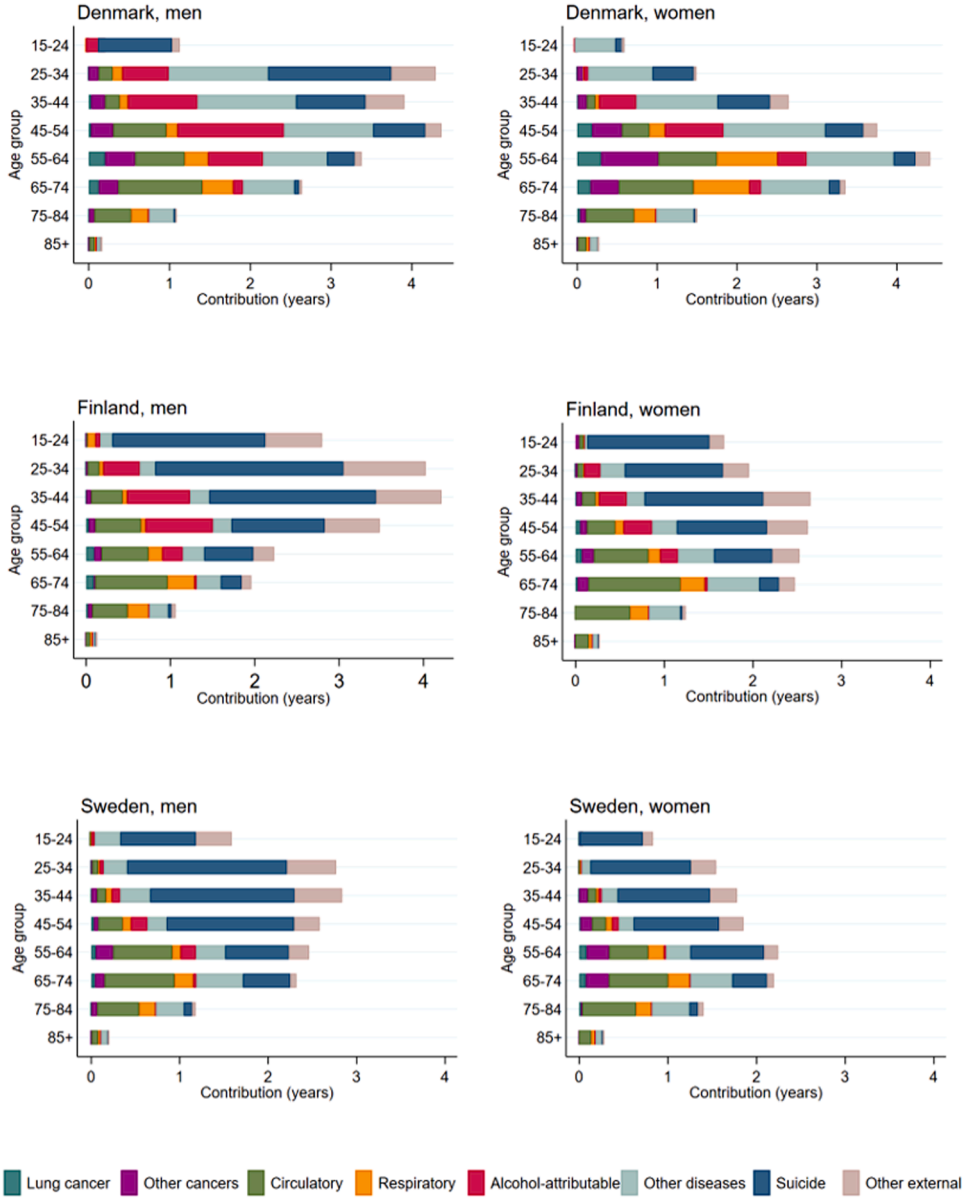


**Fig. 1.** Decomposition of the gap in life expectancy at age 15 years for psychiatric inpatients with depression by cause of death and age group, men and women in Denmark, Finland and Sweden, 1993 to 2007.

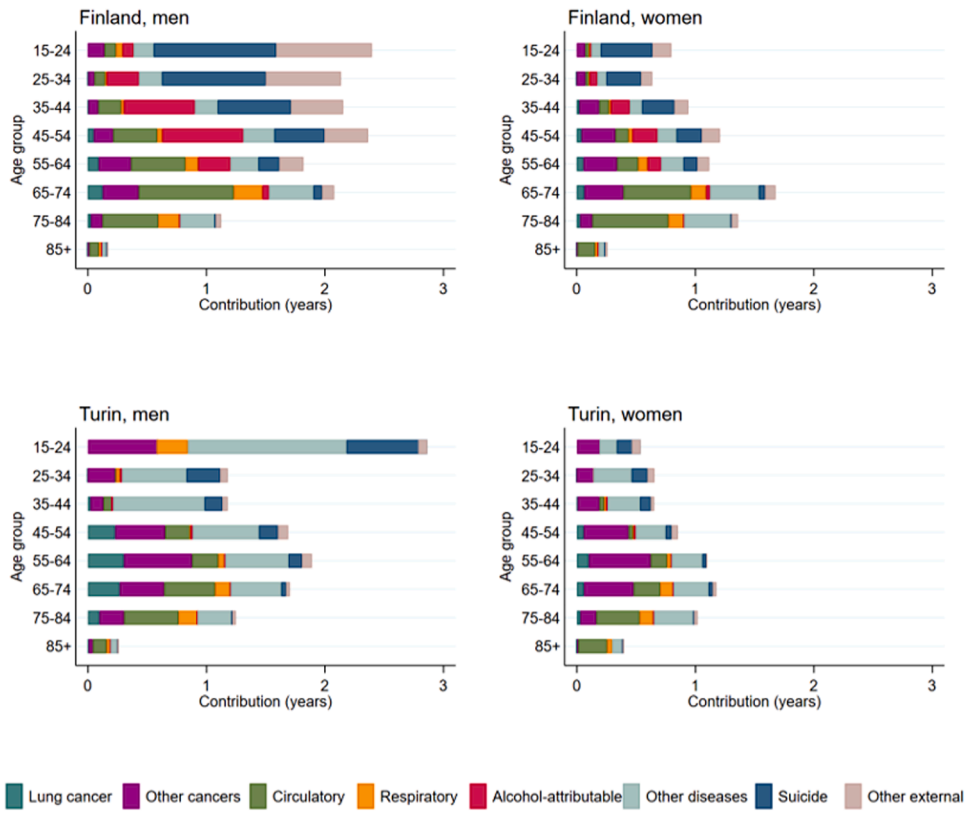


**Fig. 2.** Decomposition of the gap in life expectancy at age 15 years for antidepressant-treated outpatients by cause of death and age group, men and women in Finland and Turin, Italy, 2000 to 2007.

severe depression requiring psychiatric inpatient care, we carried out sensitivity analyses on the Finnish data excluding those who had also had a psychiatric inpatient care episode. Using this definition of depression, the gap in life expectancy was slightly smaller: 13.4 years for men and 7.3 years for women (vs. 14.2 and 8.0 years, respectively, in the main analyses). No significant differences were observed in the age-decomposition of this gap, but the contribution of suicide was somewhat smaller, yet still substantial (2.6 years [20%] for men and 1.0 years [13%] for women). The results of the sensitivity analyses are available in the Supplementary Tables S5 and S6 and Supplementary Figure S1.

## 4. Discussion

### *4.1. Main results*

The life expectancy of people with depression was substantially lower compared to people without depression. The gap in life expectancy at age 15 years ranged from about 6 to 21 years, the gap being larger for psychiatric inpatients with depression than for antidepressant-treated outpatients. The gap was consistently larger for men than women, and in Denmark and Finland compared to Sweden or Turin. The shorter life expectancy of psychiatric inpatients with depression was predominantly due to unnatural and alcohol-attributable deaths at younger ages. By contrast, natural deaths at older ages, cardiovascular and cancer deaths in particular, contributed most to the life expectancy gap for antidepressant-treated outpatients.

To our knowledge, this is the first study to estimate the gap in life expectancy in depression in the Southern European context, our results showing a smaller gap for antidepressant-treated outpatients in Turin than in Finland. For Denmark, Finland and Sweden, our estimates are in line with those previously reported for psychiatric in- and outpatients combined in Denmark (Laursen et al., 2016) and West Australia (Lawrence et al., 2013), and for inpatients with recent-onset affective disorder in Denmark, Finland and Sweden (Nordentoft et al., 2013).

Unnatural causes of death had the largest contributions to the life expectancy gap for psychiatric inpatients, especially in Finland and Sweden. In these countries, suicide alone contributed about 5 to 8 years, which was around 40% of the total life expectancy gap. Psychotic features of depression, suicidal ideation and suicide attempt are strong predictors of psychiatric hospital placement and thus psychiatric inpatients are a select population with high risk of suicide mortality. A high risk of suicide after psychiatric hospital discharge has been documented by several studies (Aaltonen et al., 2018; Nordentoft et al., 2013; Swaraj et al., 2019). For antidepressant-treated outpatients, the contribution of suicide was smaller, likely because antidepressants are prescribed also for milder and more transient episodes of depression with a lower risk of suicide. Nevertheless, suicide contributed more than three years to the lower life expectancy of Finnish men with antidepressant-treated depression, potentially reflecting the higher overall level of suicide mortality or greater severity of depression at the time of healthcare contact among Finnish men compared to women. The smaller contribution of suicide in Turin compared to Finland reflects the low general level of suicide mortality in Italy (Bernal et al., 2007; Vichi et al., 2010).

Alcohol-attributable causes were also significant contributors to the life expectancy gap, especially in Denmark and Finland, both countries with high overall alcohol mortality (Mackenbach et al., 2015). In Finland, alcohol-attributable causes contributed to the gap similarly for psychiatric inpatients and antidepressant-treated outpatients. Alcohol use disorder is a common comorbid condition in major depression (Hunt et al., 2020) and should thus be better recognized and treated already in primary care settings to decrease mortality in depression.

The large contribution of unnatural deaths and alcohol-attributable causes among psychiatric inpatients and antidepressant-treated outpatient men in Finland was due to excess mortality at ages below 55 years. Although this pattern was even more pronounced in Finland and Sweden

than in Denmark, it is in agreement with findings from a previous study reporting particularly high excess mortality due to unnatural causes at ages below 60 years among Danish patients with severe depression (Laursen et al., 2016). The shorter life expectancy of psychiatric inpatients with depression thus seem to be driven by excess mortality in the younger age groups primarily due to unnatural and alcohol-attributable causes.

By contrast, the shorter life expectancy of antidepressant-treated outpatients in Turin and outpatient women in Finland was predominantly attributable to natural causes at older ages. For Finnish women, the largest contributions were observed for circulatory deaths above age 65 years. The association between depression and cardiovascular disease and mortality has been shown in several previous studies (Gan et al., 2014; Hemingway and Marmot, 1999). Depression is associated with several cardiovascular risk factors such as smoking (Weinberger et al., 2017), hypertension (Meyer et al., 2004; Nabi et al., 2011) and diabetes (Ali et al., 2006; Vancampfort et al., 2015), as well as physiologic changes including hypothalamic-pituitary-adrenal (HPA) axis hyperactivity, cardiac rhythm disturbances and inflammation (Carney et al., 2005; Joynt et al., 2003), which all increase the risk of cardiovascular death (Wang et al., 2006). The prognosis of cardiovascular disease has also been shown to be poorer for patients with depression compared to those without (Yang et al., 2018), which may relate to physiologic factors (Joynt et al., 2003) as well as noncompliance with treatment (DiMatteo et al., 2000; Wang et al., 2002). Interventions that mitigate these pathways are thus important for increasing the life expectancy of people with less severe (antidepressant-treated) depression.

In Turin, cancers and the category of 'other diseases' had the largest contributions to the life expectancy gap. Smoking is undoubtedly the most important link between depression and lung cancer deaths and is known to be highly prevalent in Italy, specifically in urban areas (Gallus et al., 2011; Idris et al., 2007). Apart from smoking depression may also increase cancer incidence and death through other health behaviors such as alcohol consumption, unhealthy diet and physical inactivity (Gotay, 2005), noncompliance with treatment (DiMatteo et al., 2000), and chronic inflammation (Currier and Nemeroff, 2014). Previous studies have also reported higher mortality for cancer patients with depression (Pinquart and Duberstein, 2010; Yang et al., 2018). Depression is also a common comorbidity with longstanding somatic illness. For example, about 15 to 25% of cancer patients have been estimated to have comorbid depression (Chochinov, 2001), and about 10 16% of cancer patients are treated with antidepressants (Sanjida et al., 2016), the proportion being somewhat larger in terminal patients (Brelin et al., 2013; Ng et al., 2013). It is thus important to note that our analysis does not imply a particular causal direction between depression and somatic disease.

### 4.2. Strengths and limitations

This study employed large-scale population-representative register data from Denmark, Finland, Italy and Sweden to investigate the contributions of different causes of death to the gap in life expectancy in depression. The data avoids non-response and attrition thus including also the most vulnerable or marginalized sub-populations that are often hard to reach in survey studies (Fischer et al., 2001). Furthermore, register data is not subject to recall bias or misreporting. However, we also acknowledge the limitations of this study. The individuals identified as having depression sought treatment for their depression. Previous studies from Finland have indicated that less than a third of people with depression used healthcare services for the disorder (Hämäläinen et al., 2004) suggesting that the sensitivity of our depression measure is rather low. Furthermore, the Italian data only covered antidepressant prescriptions by general practitioners and public specialists, in which case the medications are free of charge and, thus, all prescriptions by private physicians remained undetected. To the extent that this brings bias to our estimates, it should bias our results towards the null. Antidepressants are also used for non-psychiatric conditions, especially in the older population (Sihvo et al., 2008). In particular, the use of antidepressants to treat neuropathic pain (Verdu et al., 2008) may lead us to overestimate the contribution of cancer and other disease mortality to the excess mortality in depression. Nevertheless, in the general adult population about 60% of antidepressant users have a history of depression and 75% at least some psychiatric indication (Sihvo et al., 2008). The high prevalence of psychiatric indications is likely reflected in our results, as the cause-of-death structure is very similar for psychiatric inpatient and antidepressant-treated outpatient men in Finland.

Another limitation is that the coding practices of the cause of death and the general quality of vital statistics differ across countries. Misclassification of suicides (Kapusta et al., 2011) and ill-defined and unknown causes of death (Ylijoki-Sørensen et al., 2014; Juel and Sjøl, 1995) in particular may bias cause-specific analyses especially for countries with low autopsy rates. In the Nordic countries, the autopsy rate is particularly low in Denmark (Kapusta et al., 2011; Ylijoki-Sørensen et al., 2014). It is thus possible that the smaller contribution of suicide and the particularly large contribution of 'other diseases' in Denmark compared to Finland and Sweden partly relate to such misclassification. Unfortunately, official data on autopsy rate in Italy is not available, yet reportedly, the majority of violent deaths are certified without autopsies (Di Vella and Campobasso, 2015). Furthermore, relying only on the underlying cause of death likely underestimates the real contribution of alcohol to the life-expectancy gap in all countries.

Finally, the life table method assumes that individuals with depression experienced the age-specific mortality rates observed for the depressed throughout their life. It is indeed the case that people with lifetime depression experience considerably higher mortality rates at all ages. However, the life expectancy estimates that we present are likely to overestimate mortality for many people who experience sporadic or intermittent episodes of depression. Therefore, our estimates – as well as those reported in previous studies – should be interpreted as an upper limit of the mortality gap in depression.

### 4.3. Conclusions

Our investigation on psychiatric inpatients highlights that intervention efforts should be directed to self-harm and substance use problems among younger patients with severe depression. By contrast, with antidepressant-treated outpatients and with older patients in particular, special attention should be addressed to rigorous monitoring and treatment of comorbid somatic conditions and disease risk factors to decrease cardiovascular and cancer mortality. This study also demonstrates that effective measures may be specific to the country context: actions against cancer mortality should be taken in Italy in particular, while prevention of alcohol-attributable mortality would have a larger population-level impact in Denmark and Finland, and of suicide in all three Nordic countries.

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## CRediT authorship contribution statement

**Kaarina Korhonen:** Methodology, Formal analysis, Writing – original draft, Writing – review & editing. **Heta Moustgaard:** Writing –

review & editing. **Lasse Tarkiainen:** Writing – review & editing. **Olof Östergren:** Data curation, Writing – review & editing. **Giuseppe Costa:** Data curation, Writing – review & editing. **Stine Kjaer Urhoj:** Data curation, Writing – review & editing. **Pekka Martikainen:** Data curation, Writing – review & editing.

## Declaration of Competing Interest

All authors declare they have no conflicts of interest.

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2021.08.076.

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