**Informative title: Depression and neuroticism decrease among women but not among men between 1976-2016 in Swedish septuagenerians**

**Running title: Depression and neuroticism decrease among women**

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**Conflict of interest**

None.

**Description of authors’ contributions**

Resources and supervision: IS (senior author), MW. Formal analyses: TRS, NS. Writing – original draft preparation: TRS, IS. Writing – review and editing: TRS, PG, RS, FA, NS, AZ, SK, SÖ, MW, IS.

**Data Accessibility Statement**Any data not published and supporting the results within the article are available from the corresponding author upon reasonable request.

**ABSTRACT**

**Objectives**: We evaluated birth cohort differences in depressive symptom burden, prevalence of depression diagnoses, and neuroticism, among Swedish 70-year-olds examined between 1976 and 2016.

**Methods**: We used a repeated cross-sectional design examining four representative population samples of Swedish 70-year-olds (total n=2279) with identical methods in 1976-77 (n=392), 1992-93 (n=226), 2000-02 (n=487), and 2014-16 (n=1166). Depressive symptom burden was rated with the Montgomery Åsberg Depression Rating Scale. Major depression was diagnosed according to DSM-5, and minor depression according to DSM-IV-TR research criteria. Neuroticism was rated with the Eysenck Personality Inventory.

**Results**: For women in 2014-16, MADRS score (4.4 vs. 6.1 vs. 5.8; *p*<0.05) and neuroticism (6.6 vs. 7.7 vs. 9.2; *p*<0.05) were lower compared to 1992-93 and 1976-77, and the prevalence of any depression was lower compared to 2000-02 and 1992-93 (10.9% vs. 16.9% vs. 18.1%; *p*<0.05). For men, we observed no birth cohort differences in depression, while neuroticism was found to be lower in 2014-16 compared to 1976-77 among men without depression (5.1 vs. 5.9; *p*<0.01). The sex difference for MADRS and neuroticism declined between 1976-77 and 2014-16 (cohort\*sex *p*<0.05).

**Conclusions**: Depressive burden and neuroticism decreased in 70-year-old women between 1976 and 2016.

**Keywords**: Depression; epidemiology; gender; old age; public mental health

**Significant Outcomes**:

* Projections for depression rates in the population are uncertain as the prevalence may change over time and may differ between birth cohorts. Our results show fluctuating prevalence between 1976 and 2016, however a decrease only statistically significant for women.
* Our findings show a decreased sex ratio in depression and neuroticism between 1976 and 2016, suggesting that environmental factors may play a role when contradicting time trend results for men and women are reported among studies.

**Limitations**:

* The 1922 birth cohort only includes women, which limited our ability to investigate time trends in men to the same extent.
* Some sub-groups in our analyses (e.g men and women with major depression) were small, which limited the statistical power and may have generated false negative results.

**INTRODUCTION**

Depression is one of the most common mental disorders in old age 1, and the leading cause of global burden of disease in both men and women 2. Although prevalence estimates vary among studies 3, a consistent finding is that the prevalence of depression is about twice as high among women compared to men 4. Among older populations (> 65 years), the prevalence of depression is approximately 10% 5, including 4-5% with major depression 1. According to the population-based Swedish National Study on Aging and Care in Kungsholmen (SNAC-K), the prevalence of depression is 5.9% among persons above age 60 (major depression: 0.8%, minor depression: 5.1%) 6, while the Survey of Health, Ageing and Retirement in Europe (SHARE) report a prevalence of 19.9 % among persons (>50 years) living in Sweden 7. Compared to younger age groups, depression seems to have stronger association with suicide in older persons 8.

As populations are ageing world-wide 9, most of the projected gains in life expectancy will occur among those above age 65 years 10, making late life depression an escalating public health problem. The global prevalence of major depression for all ages and both sexes combined has been shown to increase 11. However, age- and sex-specific projections are uncertain as the prevalence of depression may change over time 12. An increase in depression is suggested for younger 13, and middle-aged 14 populations. Among older adults the prevalence of major depression has been found to be stable 15, while milder forms of depression have been reported to increase 16, decrease 12 or fluctuate 17 over time. Studies also show inconclusive time trend results 18. Few studies have examined time trends beyond 2010.

Neuroticism is a personality factor that is strongly related to depression, especially in late life 19. It is also more common in women compared to men 20. Potential time trends in neuroticism may thus influence the prevalence and incidence of depression 21. However, it is not clear whether the association between neuroticism and depression among older people changes across subsequent birth cohorts. Previous studies in younger samples have reported higher neuroticism in later born cohorts 22, while studies in older samples 23 report no birth cohort differences. In relation to the life-course perspective, it has been reported that there is a decrease in neuroticism with age during adulthood 24, while there are no age-related changes in neuroticism from mid- to late life 25.

The study of time trends in depression involves a number of methodological challenges. Studies should include representative population-based samples undergoing personal examinations, as register data (such as health care registers or prescription data) may be influenced by changes in awareness of depression among clinicians and patients. In addition, register studies only captures those seeking help at health care facilities, and only a minority of persons with depression are detected by the health care system. Examinations also need to be identical over time. These criteria are fulfilled in the Gothenburg H70 Birth Cohort Studies (the H70 study), which have been conducted over more than four decades.

Studies on time trends in depression can provide a dynamic view of population mental health over time. It can thus generate hypotheses for further research regarding the role of underlying factors for depression in the older population (e.g. regarding environmental factors or gender roles), which may have importance for creation of preventive programs and means of treating depression, but also be utilized in planning of psychiatric healthcare, need assessments, service planning and policy development. It can also give clues regarding the ability of the health care system to detect and treat depression, and whether this has changed over time.

We have previously reported that several factors related to depression in older age have changed during the last decades, such as improvement in cognitive function 26, lung function 27, cardiovascular health 28, sexual activity 29, and decrease in the prevalence of dementia 30,31. We therefore hypothesized that the burden of depressive symptoms and the prevalence of depression would be lower for both sexes in later-born cohorts. We further hypothesized that this change would be particularly pronounced in women due to the reported increase in gender equality 32. Due to the strong association with depression, a lower level of neuroticism could also be expected.

**Aims of the study**

The first aim of this study was to explore birth cohort differences in burden of depressive symptoms, and prevalence of depression in representative samples of Swedish 70-year-olds examined with identical methods in 1976-77, 1992-93 (only women), 2000-02 and 2014-16, and whether time trends differed between sexes. Second, to further strengthen the evaluation of birth cohort differences in depression, we also examined time trends in neuroticism, and whether its relation to depression changed over time.

**METHODS AND MATERIALS**

**Participants**

The participants originate from the Gothenburg H70 Birth Cohort Studies in Sweden (the H70 studies) 33. Eligible participants were systematically sampled from the Swedish Population Register based on birth dates, and included persons living in both private households and residential care. In this study, examinations of 70-year-olds conducted in 1976-77 (birth cohort 1906-07), 1992-93 (birth cohort 1922, women only), 2000-02 (birth cohort 1930) and 2014-16 (birth cohort 1944) were included.

**Examination 1976-77 (birth cohort 1906-07):**In 1976-77, all 70-year-olds living in Gothenburg and born between July 1st, 1906 and June 30th 1907 on birth dates ending with 2, 5 or 8 were invited to participate (n=1281). All participants were numbered from 1 to 5. Those with number 1 or 2 were invited to take part in a psychiatric examination (n=513). Out of these, 404 (177 men and 227 women) participated (response rate 78.8%) 34. In this paper, participants for whom depression diagnosis could not be established due to missing data (n=5) and participants with dementia (n=7) were excluded, leaving 174 men and 218 women for analyses (n=392).

**Examination 1992-93 (birth cohort 1922):**In 1992-93, all 70-year-old women living in Gothenburg and born during 1922 on birth dates 6, 12, 18, 24 or 30 were invited to participate (n=473). A total of 299 participated (response rate 63.2%) 35. Out of these, 236 women took part in the psychiatric examination. In this paper, participants for whom depression diagnosis could not be established due to missing data (n=2) and participants with dementia (n=8) were excluded, leaving 226 women for analyses.

**Examination 2000-02 (birth cohort 1930):**In 2000-02, all 70-year-olds living in Gothenburg and born during 1930 on birth dates: 3, 6, 12, 18, 21, 24, or 30 were invited to participate (n=753). A total of 524 participated (response rate 70%). Out of these, 499 (229 men and 270 women) took part in the psychiatric examination. In this paper, participants for whom depression diagnosis could not be established due to missing data (n=4) and participants with dementia (n=8) were excluded, leaving 227 men and 260 women for analyses (n=487).

**Examination 2014-16 (birth cohort 1944):**In 2014-16, all 70-year-olds living in Gothenburg and born during 1944 on birth dates ending with 0, 2, 5 or 8 were invited to participate (n=1667). A total of 1203 participated (response rate 72.2%) 36. Out of these, 1194 (555 men and 639 women) took part in a psychiatric examination. In this paper, participants for whom depression diagnosis could not be established due to missing data (n=9) and participants with dementia (n=19) were excluded, leaving 542 men and 624 women for analyses (n=1166).

**Study Procedures**

The examinations were conducted at an outpatient clinic or in the participant’s home, and comprised comprehensive social, somatic, cognitive, functional, and psychiatric examinations, as well as close informant interviews and a battery of laboratory tests. All examinations were performed by psychiatric health professionals using identical methods over four decades to enhance possibilities of birth cohort comparisons.

The H70 studies were approved by the Ethics Committee for Medical Research at the University of Gothenburg 1976-2002, and by the Regional Ethical Review Board in 2014. Informed consent was obtained from all participants or their close relatives, and the study was conducted according to the Helsinki Declaration.

**Psychiatric examination**

The psychiatric examination comprised a semi-structured interview conducted by psychiatrists in 1976-77 and 1992-93, by psychiatric research nurses in 2000-02, and by psychiatric research nurses, psychiatrists or medical doctors in 2014-16. The psychiatric nurses and medical doctors who performed the examinations from 1992-93 to 2014-16 were trained by a psychiatrist (IS) who, in turn, was trained by the psychiatrists who performed the psychiatric examinations in 1976-77. Interrater reliability 37 was assessed in 50 individuals who had dual ratings by either psychiatric nurses or psychiatrists. K values for the presence versus absence of symptoms and signs necessary to diagnose depression were between 0.62 and 1.00 indicating “good” (reference range K = 0.61-0.80) or “excellent” (K = 0.81-1.00) agreement 16.

The psychiatric examination comprised ratings of psychiatric symptoms and signs experienced in the past month according to the Comprehensive Psychopathological Rating Scale (CPRS) 38, which has good reliability among older persons 39. Depressive symptom burden was rated according to the Montgomery-Åsberg Depression Rating Scale (MADRS) 40. MADRS is a subscale of the CPRS and include 10 items representing depressive symptoms. Individual items were rated from 0 (no symptoms) to 6 (severe symptoms), generating a MADRS-score ranging between 0-60. MADRS has been found to be valid among older populations 41.

**Neuroticism**

The Eysenck Personality Inventory (EPI) comprises 57 self-rating questions (yes/no) and is designed to measure the personality dimensions extraversion–introversion and neuroticism-stability 42. Neuroticism score ranges between 0-24. High scores represent emotional overreaction combined with low ego-strength, guilt proneness, anxiety and psychosomatic concerns. EPI data was not collected in 2000-02 (birth cohort 1930).

**Diagnoses**

*Depression*

Depression diagnoses were established using computerized symptom algorithms based on the CPRS, retrospectively applied to the responses from the psychiatric interviews at all examinations (1976-77, 1992-93, 2000-02 and 2014-16), in accordance with previous analyses from the H70 studies 43.

Major depression was diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) 44, and required the presence of at least 5 out of 9 pre-specified depressive symptom clusters during the last month, of which at least one had to be depressed mood or diminished interest/pleasure. Minor depression was diagnosed according to DSM-IV-TR research criteria 45 and required the presence of 2–4 of the same pre-specified symptoms as for major depression. For the purpose of this paper, the term “any depression” was used to denote those fulfilling criteria for either major or minor depression.

*Dementia*

The diagnosis of dementia was used for exclusion in the main analyses, due to the difficulty of diagnosing depression when dementia is present. We were not able to diagnose dementia according to DSM criteria in 1976–77. To enable comparisons between the four examinations, dementia was instead diagnosed according to criteria described by Kay et al 46. These criteria were widely used in the 1970s and required the presence of severe disorientation in time or place or severe memory impairment as assessed during the psychiatric examination. In 2000-02, we were able to diagnose dementia according to both the old criteria and DSM-III-R 47. The observed agreement between the two classification systems was high (K = 0.81) 48.

**Demographic factors**

All demographic factors are based on self-reported information. Educational level was defined as ‘compulsory’ (i.e. ≤ 6 years in those born 1906-07 and 1922, ≤ 7 years in those born 1930, and ≤ 9 years in those born 1944) vs. ‘more than compulsory’. Regulations for mandatory years in Swedish primary schooling have changed several times during the 20th century, leading to different cut-off points for educational level in this study. Type of residence was categorized as ‘sheltered accommodation’ vs. ‘private household’. We also asked if the participant was living alone or not. ‘Having partner’ included married, having non-cohabiting partner, and having cohabiting partner. We also asked if the participant had a happy relationship, if they had children, if they felt lonely, and if they had lost their partner during last 5 years due to death or divorce. All participants were asked to report their medications, doses and indications for treatment. Antidepressants (N06A) were classified according to the Anatomical Therapeutic Chemical (ATC) classification system recommended by the WHO 49. We also asked if the participant was experiencing back or joint pain (joint pain also included stiff or swollen joints). Having contact with health care included contact with medical doctor or nurse at any health care facility or during home visit during the last 3 or 12 months.

**Statistical Analysis**

Pearson’s Chi-square was used to test differences in proportions. To compare differences in group means in MADRS and neuroticism score, we utilized the Analysis of Variance (ANOVA) statistical model with the flexibility to perform post-hoc Tukey test. Independent samples t-tests were used to test sex differences in mean scores. A univariate Generalized Linear Model (GLM) was used to check for potential effect modification by sex on birth cohort differences in mean MADRS score and mean neuroticism score, where the interaction term sex\*birth cohort was added, and for potential effect modification by neuroticism on sex differences in depression, where the interaction term neuroticism\*sex was added. A binary logistic regression (crude odds ratios with 95 % confidence intervals) was used to test differences by birth cohort and sex in the prevalence of major, minor and any depression, and to check for potential effect modification by sex on birth cohort differences in depression, where the interaction term sex\*birth cohort, was added.

Binary logistic regression was used to test for possible associations between mean neuroticism score and major, minor, and any depression. A linear regression model was used to test for possible association between mean neuroticism score and mean MADRS score.

Sensitivity analyses using log-transformed values (log10) for MADRS were performed, supporting the results by reducing the effects of outlying observations in the MADRS score. Sensitivity analyses not using dementia as exclusion criteria were performed for all birth cohort comparisons in depression and neuroticism, supporting the results. Statistical methods were carried out using IBM SPSS STATISTICS 22. All statistical tests were two-tailed and p-values of <0.05 were considered statistically significant.

**RESULTS**

Sample characteristics of 70-year-olds examined 1976-77, 1992-93, 2000-02 and 2014-16 are presented in Table 1. As may be seen, the use of antidepressants was higher among later born cohorts.

(Insert Table 1)

**Burden of depressive symptoms**

Data on depression in 1992-93 were available only for women.

*Birth cohort differences in MADRS score*

As may be seen in Table 2, MADRS score was lower in 2014-16 compared to 1976-77 in the total sample. Among women, MADRS score was lower in 2014-16 compared to 1992-93 and 1976-77, but did not differ from 2000-02. No significant time trends were observed among men. Among women without depression, MADRS score was lower in 2014-16 compared to 1976-77, but was not significantly different from the other examinations. No differences were observed among men, or among those with depression.

*Interaction effect*

There was an interaction between sex and birth cohort in relation to MADRS score (B= -0.46; R2=0.02; *p*=0.02), i.e. sex differences declined, and the decrease in MADRS score at later examinations was more accentuated in women.

(Insert Table 2)

**One-month prevalence of depression**

Figure 1 shows the one-month prevalence of major, minor and any depression in 70-year-olds from 1976-77 to 2014-16.

*Birth cohort differences in depression diagnoses*

The prevalence of major depression did not differ between examinations in the total sample. The prevalence of minor depression and any depression was lower in 2014-16 compared to 2000-02. Among women, the prevalence of any depression was lower in 2014-16 compared to 2000-02 and 1992-93. The prevalence of major depression in women was lower in 2014-16 compared to 1992-93. The highest prevalence in women was observed in 1992-93. No birth cohort differences were found among men.

*Interaction effect*

There was no interaction effect between sex and birth cohort in relation to minor depression (B= -0.13; OR=0.88; *p*=0.39), major depression (B= -0.06; OR=0.94; *p*=0.82) or any depression (B= -0.12; OR=0.89; *p*=0.36).

(Insert Figure 1)

**Neuroticism**

Data on neuroticism were available only for women in 1992-1993, and data collection was not conducted in 2002-02. For 1976-77, 1992-93, and 2014-16, independent samples t-tests showed small or no difference in mean MADRS score between those having missing data on neuroticism and those who did not.

*Birth cohort differences in neuroticism*

Mean neuroticism score was lower in 2014-16 compared to 1976-77 (6.1 vs. 7.8; *p*<0.01) in the total sample. As may be seen in Table 2, neuroticism in women was lower in 2014-16 compared to both 1992-93 and 1976-77, while no significant time trends were observed among men. Among those without depression, neuroticism decreased both among women and among men. Among women with depression, neuroticism was lower in 2014-16 compared to 1976-77.

*Association between neuroticism and depression across birth cohorts*

There was an association between neuroticism and depression at all examinations. Overall, this association did not change across cohorts. The results can be seen in Supplementary Table 1.

*Interaction effect*

There was an interaction between sex and birth cohort (B= -0.64; R2=0.07; *p*<0.01), i.e. the association between sex and neuroticism score differed between examinations (the sex difference declined), and the lower neuroticism score at later examinations differed between sexes (decline only observed in women). There was a tendency towards an interaction effect between sex and neuroticism in relation to major depression in 1976-77 (OR=1.4; *p*=0.07), not reaching our set level of statistical significance, while no interaction was found in 2014-16 (OR=0.9; *p*=0.57). There was no interaction in relation to minor depression, neither in 1976-77 (OR=0.9; *p*=0.54), nor in 2014-16 (OR=1.0; *p*=0.91). There was no interaction in relation to any depression neither in 1976-77 (OR=1.1; *p*=0.41), nor 2014-16 (OR=0.9; *p*=0.93). There was an interaction effect between sex and neuroticism in relation to MADRS score in 1976-77 (R2=0.25; B=0.36; SE=0.13; *p*=0.006), while there was no such interaction in 2014-16 (R2=0.27; B=0.06; SE=0.07; *p*=0.34).

**Sex differences**

Table 3 shows sex differences in MADRS score, the prevalence of depression, and neuroticism, by examination year. Women had higher MADRS score, higher prevalence of any depression, and higher neuroticism score compared to men at all examinations. For any depression, the sex ratio was 2.6:1 in 1976-77 (*p*<0.05), 2.0:1 in 2000-02 (*p*<0.05), and 1.7:1 in 2014-16 (*p*<0.05). While no significant sex differences were observed for major and minor depression (except for minor depression in 1976-77), the female:male sex ratio ranged between 2.7:1 to 1.5:1.

(Insert Table 3)

**The use of antidepressants**

Despite an increased use of antidepressantsbetween 1976-77 and 2014-16 (4.5% vs. 9.7%; *p*<0.01) in the total sample, only a minority of persons with depression received pharmacological treatment (18.2% in 1976-77 vs. 27.7% in 2000-02 vs. 30.8% in 2014-16; *p*>0.05). The use of antidepressants among women having depression was higher in 2014-16 than in 1976-77 (39.7% vs. 18.2%; *p*<0.05), while no differences were observed among men. Birth cohort differences in antidepressant use among persons not having depression were observed in both men (1.2% in 1976-77 vs. 5.3% in 2014-16; *p*<0.05) and women (4.2% in 1976-77 and 4.9% in 1992-93 vs. 9.8% in 2014-16; *p*<0.05). Antidepressant use was more common in women compared to men at all examinations (6.3% vs. 2.3%, 13.5% vs. 3.1%, 13.1% vs. 5.9%; *p*<0.05).

**DISCUSSION**

We found that depressive symptom burden and neuroticism decreased among women but not among men between 1976 and 2016 among a population-based sample of 70-year-olds. Time trends for the diagnoses of major, minor, and any depression were less clear. The lowest prevalence for minor depression was noted in 2014-16, while that of major depression remained stable. Women still had higher burden of depressive symptoms, neuroticism and prevalence of any depression compared to men at all examinations, a global phenomenon in all age groups 2,50. However, the gender gap decreased over time.

The prevalence of depression may be influenced by how life courses are embedded in societal and geographical contexts across historical times 51, i.e. by age, birth cohort, and period effects. Disentangling birth cohort and period effects can be challenging. Birth cohort effects may have generated differences in health-related factors throughout the life course, which may be related to the proneness of depression. For example, our cohort born 1906-07 experienced starvation during World War I, food rationing during World War II, had poor living conditions during the first 3-4 decades of their lives (including poor education, working conditions and health care), while the latest born cohort of 1944 lived their lives in a modern welfare state. A period effect may be that we had the highest depression rate in 1992-93, when an economic recession took place in Sweden. As only women were examined in 1992-93, we do not know if the peak was present also for men (see Figure 2).

(Insert Figure 2)

For any depression, the sex ratio decreased from 2.6 in 1976-77, to 2.0 in 2000-02, and 1.7 in 2014-16. One possible reason for this finding may be the increasing gender equality occurring in Sweden during the 20th century 52. Later born cohorts of women have to a larger extent benefitted from societal improvements, such as women’s emancipation during the 20th century, the large expansion of governmentally funded child day care in the 1960s and 70s, the sexual revolution in the 1960s with the introduction of contraceptive pills, free abortion in the 1970s, increased quality of pre- and postnatal care, increased standard and accessibility of health care, and access to university education and paid employment. Still, due to cultural gender norms, women face a role strain overload 53, expected to manage their own work, primary household, care for children, grandchildren and spouses, even beyond retirement age. This overload has been associated with depressive symptoms in women 54, and might partly explain why the prevalence of depression and burden of symptoms still remained higher among women compared to men across our 40 year study period, in spite of societal improvements. Another factor that can be related to sex differences in depression is rumination. This is a type of repetitive negative thinking, which is reported to be both more common in women and also a risk factor for depression 55. Other suggested explanations for the higher prevalence of depression in women includes that women report symptoms more often while men do not perceive or report them 56, or the presence of biological differences, e.g. related to hormonal 57 or genetic factors 58.

Our findings highlight the importance of environmental factors. Previous studies 22 have shown that environmental factors (e.g. rates of unemployment, economic recession, or worries about climate change or terror attacks) play a large role in birth cohort differences in personality and anxiety, which are both strongly associated with depressive mood. The direction of change in environmental factors can merely be speculative, causing future time trend projections for depression in late life to be uncertain. A worrying trend is that the prevalence of depression is increasing in younger age groups 13, which might have implications for future generations of older people due to the potential risk of recurrence 8,59. However, studies also show that emotional wellbeing improves with age 60.

Some of the environmental factors displayed in Figure 2 may have affected both sexes differently (e.g. rationings during WWI and WWII, the recessions in the 1930s and 1990s, access to improved health care, or development of treatment methods for depression). As an example, a previous study showed that increased rates of unemployment due to economic recessions may affect the time trends of recorded depressions (at general practices) among men, but not among women 12. A continuing of societal improvements (e.g. increased awareness of depression that reduce stigma, changes in normative masculine gender roles allowing men to recognize and express depressive symptoms, enhanced treatment efficacy, increased equality in legal rights and societal position for men and women) and improved life conditions (e.g. life expectancy, burden of disease), may generate a further reduction in the sex ratio of depression. The reason why we do not find any time trends in the prevalence of depression among men may not primarily be due to less significant benefits from societal improvements (compared to the benefits that women may have gained), but also partly due to small sample sizes, or consolidated masculine gender roles still connected to the under-reporting of depressive symptoms. However, the higher prevalence of depression among women (compared to men) is so far a robust finding irrespective of time period, age of samples, and geographical settings.

Results on time trends and birth cohort differences of depression may vary between studies depending on examination years, time spans, birth cohorts, age ranges, and geographical areas. Also, contradicting results between studies can be due to the use of different instruments and diagnostic criteria, which previously has been shown in a Swedish study of older adults 61. The only change between DSM-III/DSM-IV and DSM-5 is that bereavement is no longer an exclusion criterium for a diagnosis of depression. However, in our study, diagnoses were made (using retrospectively applied symptom-based algorithms) according to DSM-5 (major depression) and DSM-IV-TR research criteria (minor depression) at all examinations (1976-77, 1992-93, 2000-02 and 2014-16) in order to increase comparability.

Few studies on time trends in depression among older persons have so far extended beyond 2010. Several recent studies extending into the 2000s and 2010s report declining frequency of minor or any depression among older persons 5,12. A Dutch study on 55-65 year-olds reported a decrease in past-year subthreshold depression (comparable to minor depression in our study) between 2002 and 2012 for both sexes combined, but an increase in major depression from 1992 and 2002 14. Studies on major depression among older persons conducted during the same period report stable prevalence 15,16,62. In contrast, time trend studies focusing mainly on younger and middle-aged populations generally report higher prevalence of depression and depressive symptoms among later born cohorts 13,14,17,54,63-66, but the prevalence is also reported to be stable over time 67,68.

We have previously reported an increase in the prevalence of minor depression among 75-year-olds between 1976–77 and 2005–06 16. Reasons for this contrasting finding may be the older age (75 vs. 70), and that the cohort born 1930 was compared with a cohort born 1901-02. In our present study, the lowest prevalence was observed in the cohort born 1944. We could not confirm previous findings suggesting that persons born after World War II have higher prevalence of depression than those born earlier in the 20th century (age >18 years) 69-71. One reason could be that these studies were performed in the US during the 1980s and 90s, when our cohort born 1944 was only about 40 years old. It should be noted that frequency of depression may fluctuate over time and between birth cohorts, as described in a study from US and Canada in 1997-2010 17. Few other studies have a time span of more than four decades 68,72,73, and these only extends into the 1990s. Among studies with large time spans, the Stirling County Study in Canada, conducted 1952-1992, reported a stable prevalence of depression over time 68, and the Lundby Study conducted 1947-97 reported a decreasing incidence of depression in 1972-1997 compared to 1947-1972 73.

The life expectancy has increased between 1976 (approximately 72 for men and 78 for women) and 2014 (approximately 80 for men and 84 for women) 74. Depending on the general health status of the aging population, increased life expectancy may be associated with both higher and lower prevalence of depression. A higher life expectancy may increase the prevalence of depression later in life as more people with depression survive to older ages. On the other hand, a higher life-expectancy may be a reflection of better health, which may lead to lower prevalence of depression. In addition, if the relative life-expectancy increases more in people without depression than in those with depression, the prevalence will also decrease. Previous findings derived from the Gothenburg H70 Birth Cohort Study show improved health status for successive birth cohorts 26-30. Therefore, the increased life expectancy and improved life conditions in Sweden may partly be a reason for the declining prevalence of depression among 70-year-olds.

We also noted a decline in neuroticism measured with a self-rating scale between 1976-77 and 2014-16. It has been suggested that neuroticism and depression share etiological factors 75,76, and may therefore be affected by similar birth cohort effects. In support of this, we found a strong association between neuroticism and depression at all examinations, in line with previous studies 19,77. This association did not differ by birth cohort. Our finding of lower neuroticism score in later born birth cohorts support the finding of a lower prevalence of depression in 2014-16, as data collection methods differ (self-report questionnaire vs. psychiatric interview). However, it can be discussed whether the lower score of neuroticism is the reason for the lower burden of depressive symptoms, or vice versa. The direction of this association cannot be determined from this repeated cross-sectional study. However, we have previously reported that neuroticism predicts later episodes of depression among older persons 21. It could be noted that neuroticism also decreased among persons without depression.

Although not the main focus of this paper, we also analyzed birth cohort differences in the use of antidepressants to have the full picture of depression in the population. The introduction of second generation antidepressants constitute a possibly important period or birth cohort effect, although we acknowledge that our study cannot estimate to what extent this has causally influenced the prevalence of depression. As expected, we found increased use of antidepressants after the 1990s, with a stable prevalence after 2000, in line with a Canadian study 1994-2012 78. Paralleling previous studies, we found that the majority of persons with depression were not using antidepressants 6,67,79. However, treatment rate for depression increased substantially between 1976-77 and 2014-16 (from 18% to 40%) in women with depression, but not in men. Increased treatment rate may indicate an increased detection rate of depression in women in the health care system, or that physicians are prescribing for broader indications among women than previously. The sex difference may also be due to non-compliance among men, that men have other treatments for depression, or that they had not yet sought help within the health care system. We cannot elucidate if antidepressants have been prescribed for treating depression, if its increased use is the reason for the lower prevalence of depression, or if treatment with newer antidepressants may be more or less effective. Also, there is a possibility that some persons on antidepressants at the time of the examination have previously fulfilled criteria for depression and have been successfully treated. It has been suggested that increasing rates of antidepressant treatment (since the introduction of SSRI in the 1990s) has led to a decrease in suicide rates in Sweden 80. This is, however, debated 81, and may not have influenced suicide rates among older persons.

**Strengths and limitations**

Among strengths in this study are the comprehensive personal examinations of representative samples using identical methods over 40 years, that diagnoses of depression are based on psychiatric examinations conducted by psychiatrists and psychiatric nurses using structured interviews, and the use of computerized algorithms to diagnose depression, which minimizes effects of altered routines for clinical evaluations and shifting diagnostic boundaries. Also, this procedure is less influenced by potential changes in awareness of depression and help-seeking behaviors compared to information collected from registries or health records. In addition, our diagnoses are based on past month symptoms, which reduces recall bias 82.

There are also some limitations. First, the study was conducted in a mainly Caucasian Swedish sample, and our results are foremost compared with studies conducted in high income countries, since birth cohort comparisons of depression among older populations are rare in other parts of the world. We can therefore not generalize to other populations. Second, despite fairly high response rates at each examination, we cannot exclude the possibility of different time trends among participants and non-responders. Third, the investigating staff has altered between psychiatrists, psychiatric nurses, and medical doctors over the years, which to some extent could add to the differences in depression prevalence. However, all investigating staff was trained by the last author (IS), who in his turn was trained by the psychiatrists who performed the examinations in the 1970s. The high kappa value for interrater reliability indicates consistency in examinations over time. Also, neuroticism was measured using a self-rating questionnaire, while depressive symptoms were assessed during a psychiatric interview. This adds credibility to the fact that the lower burden of depressive symptoms and prevalence of any depression is not due to measurement inconsistency between staff at the different examinations. Fourth, the 1922 birth cohort only includes women, which limited our ability to investigate time trends in men to the same extent. Fifth, some sub-groups in our analyses (e.g men and women with major depression) were small, which limited the statistical power and may have generated false negative results, e.g. regarding sex differences in major depression. Sixth, comparable data on physical diseases was not available for the cohorts included in this paper. This limited our ability to analyze whether possible birth cohort differences in physical diseases may be a reason for the lower prevalence of depression in later-born cohorts. However, we take note of the fact that we have previously reported that several factors related to depression in older age have changed during the last decades, such as improvement of lung function 27, and cardiovascular health 28 in 75-year-olds born 1901-02 and 1930, improvement in cognitive function 26 and sexual activities 29 among 70-year-olds born 1901-02 and 1930, and decrease in the prevalence of dementia 30 between 85-year-olds born 1901-02 and 1923-24. Seventh, due to the difficulties in establishing reliable depression diagnosis in persons with dementia, dementia cases were excluded for all main analyses in this paper. Thus, the prevalence of depression among Swedish 70-year-olds may partly be underestimated. However, the prevalence of dementia in our samples only ranged between 0.9-3.4 %, and the results from the sensitivity analyses including dementia cases showed that this did not affect the results.

Finally, stigma for depression has decreased between the 1970s and 2010s. This might have underestimated the prevalence of depression in the oldest birth cohort.

In conclusion, our results show that depressive burden and neuroticism decreased in women between 1976 and 2016. The decreased sex ratio in depression and neuroticism in later-born birth cohorts of 70-year-olds may be due to the increasing gender equality occurring in Sweden during the period and shows the importance of considering environmental factors in the discussion on sex differences in depression.

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| **TABLE 1**.Sample characteristics of 70-year-olds by sex and examination year | | | | | | | | |
|  | **Men** | | |  | **Women** | | | |
| Examination year | 1976-77 | 2000-02 | 2014-16 |  | 1976-77 | 1992-93 | 2000-02 | 2014-16 |
| Birth cohort | 1906-07 | 1930 | 1944 |  | 1906-07 | 1922 | 1930 | 1944 |
|  | **%** (no. of cases/ total cases) | **%** (no. of cases/ total cases) | **%** (no. of cases/ total cases) |  | **%** (no. of cases/ total cases) | **%** (no. of cases/ total cases) | **%** (no. of cases/ total cases) | **%** (no. of cases/ total cases) |
| Dementia | **1.7** (3/177) | **0.9** (2/229) | **1.8** (10/552) |  | **1.8** (4/222) | **3.4** (8/234) | **2.3** (6/266) | **1.6** (10/634) |
| **N** (dementia free sample) | **174** | **227** | **542** |  | **218** | **226** | **260** | **624** |
| **Demographics** |  |  |  |  |  |  |  |  |
| > Compulsory education | **17.9** (31/173)§¶ | **43.4** (98/226)¶ | **81.1** (438/540) |  | **17.6** (38/214)‡§¶ | **38.5** (79/205)¶ | **38.3** (98/256)¶ | **85.7** (533/622) |
| Living alone | **0.6** (1/174)¶ | † | **27.2** (145/533) |  | **1.8** (4/218)¶ | † | † | **43.2** (266/616) |
| Sheltered accommodation | **0.6** (1/172) | **0** (0/227) | **0.2** (1/538) |  | **0** (0/218) | † | **0.4** (1/256) | **0.3** (2/621) |
| **Relationships** |  |  |  |  |  |  |  |  |
| Lost partnerduring last 5 years | **4.6** (8/174) | **1.3** (3/227) | **4.1** (22/542) |  | **11.0** (24/218)¶ | **11.9** (27/226)¶ | **7.3** (19/260) | **5.1** (32/624) |
| Having partner | **78.0** (135/173) | **80.6** (183/227) | **76.4** (407/533) |  | **43.6** (95/218)‡¶ | **54.2** (122/225) | **50.8** (132/260)¶ | **58.8** (362/616) |
| Happy relationship | **20.1** (35/174)§¶ | **48.9** (111/227) | **45.3** (244/539) |  | **13.8** (30/218)‡§¶ | **31.2** (68/218) | **27.6** (71/257) | **33.4** (205/614) |
| Having children | **75.1** (130/173)§¶ | **88.6** (186/210) | **86.9** (469/540) |  | **67.0** (146/218)‡§¶ | **85.5** (183/214) | **86.1** (211/245) | **86.3** (537/622) |
| Feeling lonely | **15.8** (27/171) | **17.5** (37/211)¶ | **10.4** (55/530) |  | **21.6** (47/218)§ | † | **32.2** (79/245)¶ | **22.0** (134/609) |
| **Health** |  |  |  |  |  |  |  |  |
| Antidepressant use†† | **2.3** (4/174) | **3.1** (7/227) | **5.9** (32/542) |  | **5.5** (12/218)§¶ | **8.0** (18/226)¶ | **13.5** (35/260) | **13.1** (82/624) |
| Back pain | **21.3** (37/174)§ | **36.7** (81/221)¶ | **28.5** (154/541) |  | **37.6** (82/218)§ | **44.0** (99/225) | **50.4** (127/252)¶ | **40.0** (248/620) |
| Joint pain | **12.6** (22/174)§¶ | **28.4** (63/222)¶ | **36.1** (194/537) |  | **29.4** (64/218)§¶ | **35.6** (80/225)§¶ | **48.2** (122/253) | **52.2** (320/613) |
| Visit healthcare during last 3 months | **40.8** (71/174) | **46.5** (94/202) | † |  | **52.8** (114/216) | **58.8** (124/211) | **60.0** (141/235) | † |
| Visit healthcare during last year | **64.9** (113/174)¶ | † | **91.5** (495/541) |  | **79.6** (172/216)¶ | † | † | **92.1** (568/617) |
|  |  |  |  |  |  |  |  |  |

All sample characteristics (dementia, demographics, relationships and health) have been tested for differences in proportions between examination years. Analyses of demographics, relationships, and health were based on the dementia free sample.

† Data not available for this birth cohort.

††Antidepressants (N06A) were classified according to the Anatomical Therapeutic Chemical (ATC) classification system recommended by the WHO.

‡ Significant difference compared to examination year 1992-93 (*p*<0.05)

§ Significant difference compared to examination year 2000-02 (*p*<0.05)

¶ Significant difference compared to examination year 2014-16 (*p*<0.05)

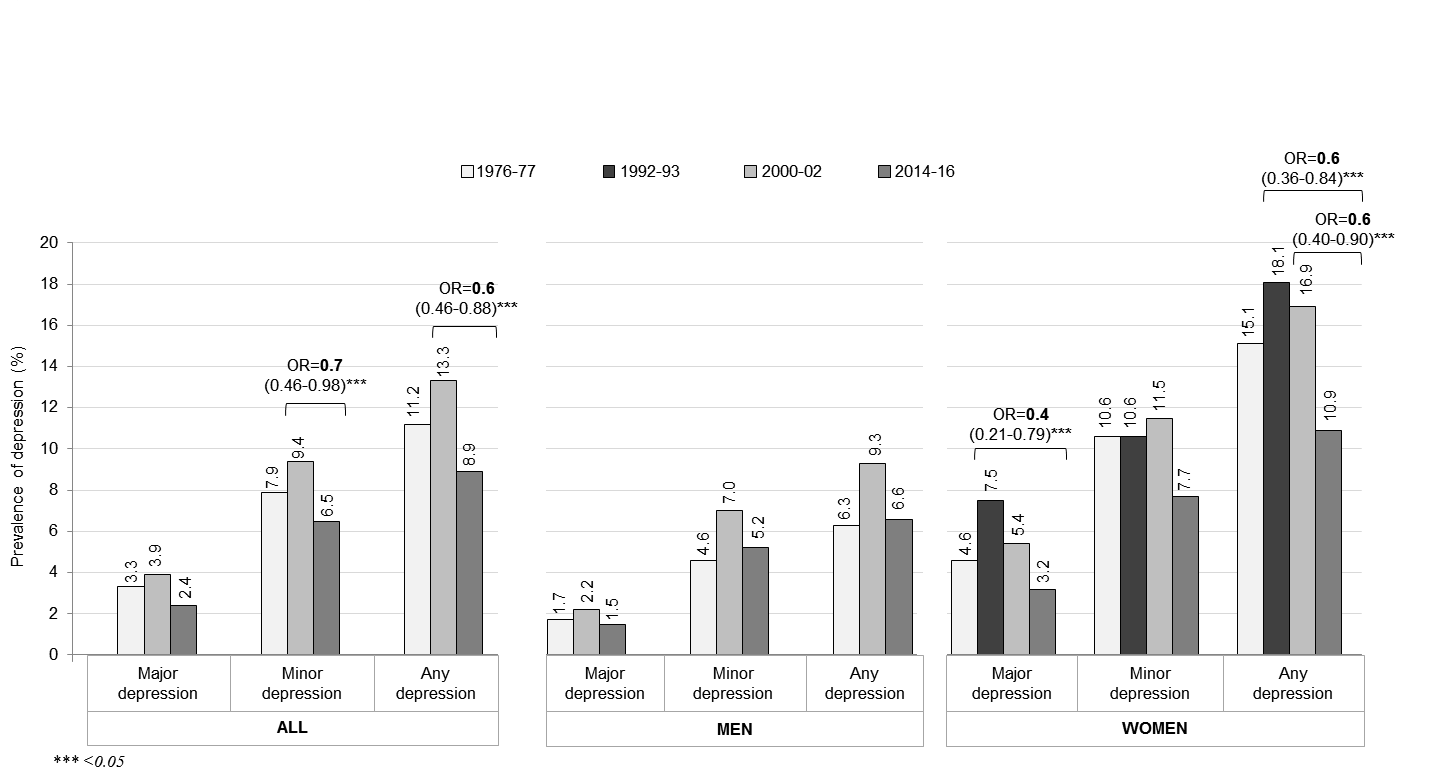
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| **TABLE 2**. Mean score of depressive symptoms and neuroticism by depression, sex and examination year/birth cohort | | | | | | | | | | | | | | |
|  | **Total sample** | | | |  | **Participants with any depression** | | | |  | **Participants without depression** | | | |
| Examination year | 1976-77 | 1992-93 | 2000-02 | 2014-16 |  | 1976-77 | 1992-93 | 2000-02 | 2014-16 |  | 1976-77 | 1992-93 | 2000-02 | 2014-16 |
| Birth cohort | 1906-07 | 1922 | 1930 | 1944 |  | 1906-07 | 1922 | 1930 | 1944 |  | 1906-07 | 1922 | 1930 | 1944 |
| **MADRS score**‡, mean(sd) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| N (men/women) | (174/218) | (†/226) | (227/260) | (542/624) |  | (11/33) | (†/41) | (21/44) | (36/68) |  | (163/185) | (†/185) | (206/216) | (506/556) |
| All | 4.8 (5.8)¶ | † | 4.6 (5.5)¶ | 4.0 (5.1) |  | 16.5 (8.3) | † | 15.1 (6.8) | 15.4 (7.2) |  | 3.3 (3.1) | † | 3.1 (3.0) | 2.9 (3.0) |
| Men | 3.6 (4.4) | † | 3.9 (4.7) | 3.6 (4.6) |  | 14.6 (7.0) | † | 14.3 (6.0) | 14.6 (7.7) |  | 2.8 (3.0) | † | 2.8 (3.0) | 2.8 (3.0) |
| Women | 5.8 (6.5)¶ | 6.1 (7.3)¶ | 5.4 (6.1) | 4.4 (5.4) |  | 17.1 (8.7) | 17.8 (8.4) | 15.5 (7.1) | 15.8 (6.9) |  | 3.8 (3.0)¶ | 3.5 (3.5) | 3.4 (3.0) | 3.0 (3.1) |
| **Neuroticism**, mean(sd) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| N (men/women) | (151/178) | (†/194) | † | (520/602) |  | (10/26) | (†/31) | † | (33/63) |  | (141/152) | (†/163) | † | (487/539) |
| All | 7.8 (4.9)¶ | † | † | 6.1 (3.9) |  | 12.5 (4.9) | † | † | 10.8 (4.4) |  | 7.2 (4.6)¶ | † | † | 5.6 (3.6) |
| Men | 6.1 (4.1) | † | † | 5.5 (3.8) |  | 8.9 (4.6) | † | † | 10.8 (4.8) |  | 5.9 (4.0)¶ | † | † | 5.1 (3.5) |
| Women | 9.2 (5.0)§¶ | 7.7 (4.1)¶ | † | 6.6 (3.9) |  | 13.9 (4.4)¶ | 12.1 (3.6) | † | 10.8 (4.3) |  | 8.4 (4.7)§¶ | 6.8 (3.7) | † | 6.1 (3.6) |

† Data not available for this birth cohort.

‡ Depressive symptoms measured with Montgomery Åsberg Depression Rating Scale (MADRS)

§ Significant difference compared to examination year 1992-93 (*p*<0.05)

¶ Significant difference compared to examination year 2014-16 (*p*<0.05)



**Figure 1.** One-month prevalence of major, minor and any depression by sex and examination year:

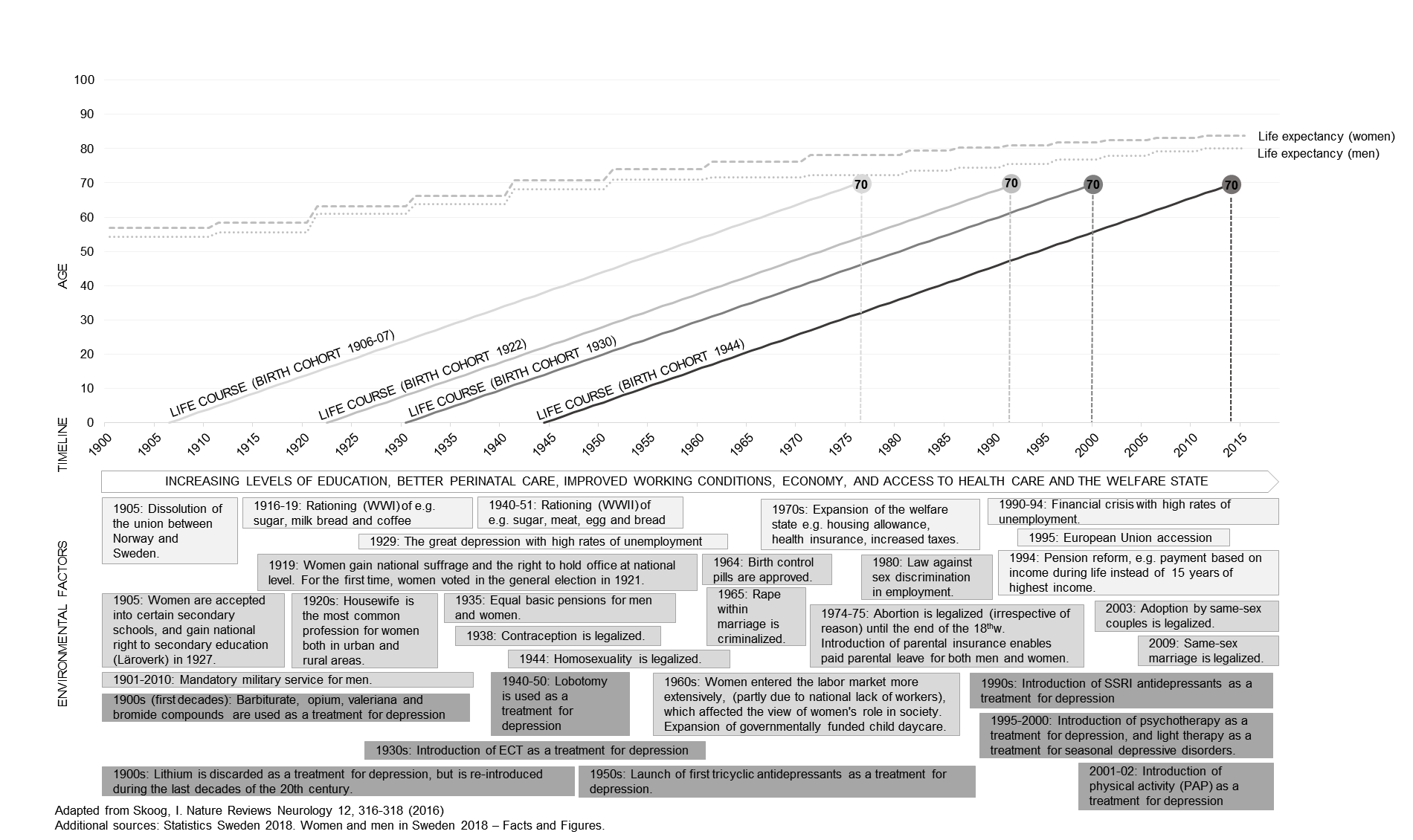
\*\*\* *< 0.05*

OR = Odds Ratio

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **TABLE 3**. Sex differences in depression and neuroticism in 70-year-olds by examination year/birth cohort | | | | | | | | |
|  |  |  |  |  |  |  |  |  |
| Examination year | 1976-77 | |  | 2000-02 | |  | 2014-16 | |
| Birth cohort | 1906-07 | |  | 1930 | |  | 1944 | |
|  |  |  |  |  |  |  |  |  |
|  | **Women vs Men** | *p* |  | **Women vs Men** | *p* |  | **Women vs Men** | *p* |
| **Total sample** |  |  |  |  |  |  |  |  |
| MADRS score (mean) | 5.8/3.6 | *\*\*\** |  | 5.4/3.9 | *\*\*\** |  | 4.4/3.6 | *\*\*\** |
| Neuroticism score (mean) | 9.2/6.1 | *\*\*\** |  | † | † |  | 6.6/5.5 | *\*\*\** |
| **Participants without depression** |  |  |  |  |  |  |  |  |
| MADRS score (mean) | 3.8/2.8 | *\*\*\** |  | 3.4/2.8 | *0.05* |  | 3.0/2.8 | *0.20* |
| Neuroticism score (mean) | 8.4/5.9 | *\*\*\** |  | † | † |  | 6.1/5.1 | *\*\*\** |
| **Participants with major depression** |  |  |  |  |  |  |  |  |
| No. of cases with major depression | (10/3) |  |  | (14/5) |  |  | (20/8) |  |
| OR, *(95 % CI)* | 2.7 (0.7-10.1) | *0.13* |  | 2.5 (0.9-7.1) | *0.08* |  | 2.2 (1.0-5.1) | *0.06* |
| MADRS score (mean) | 26.9/19.3 | *0.12* |  | 21.6/20.2 | *0.65* |  | 23.8/26.6 | *0.17* |
| Neuroticism score (mean) | 17.1/8.0 | *\*\*\** |  | † | † |  | 11.4/13.3 | *0.30* |
| **Participants with minor depression** |  |  |  |  |  |  |  |  |
| No. of cases with minor depression | (23/8) |  |  | (30/16) |  |  | (48/28) |  |
| OR, *(95 % CI)* | 2.5 (1.1-5.7) | *\*\*\** |  | 1.7 (0.9-3.2) | *0.09* |  | 1.5 (0.9-2.5) | *0.08* |
| MADRS score (mean) | 12.8/12.9 | *0.97* |  | 12.6/12.4 | *0.91* |  | 12.4/11.2 | *0.23* |
| Neuroticism score (mean) | 11.8/9.3 | *0.19* |  | † | † |  | 10.6/10.1 | *0.70* |
| **Participants with any depression** |  |  |  |  |  |  |  |  |
| No. of cases with any depression | (33/11) |  |  | (44/21) |  |  | (68/36) |  |
| OR, *(95 % CI)* | 2.6 (1.3-5.4) | *\*\*\** |  | 2.0 (1.1-3.5) | *\*\*\** |  | 1.7 (1.1-2.6) | *\*\*\** |
| MADRS score (mean) | 17.1/14.6 | *0.41* |  | 15.5/14.3 | *0.50* |  | 15.8/14.6 | *0.44* |
| Neuroticism score (mean) | 13.9/8.9 | *\*\*\** |  | † | † |  | 10.8/10.8 | *0.98* |
|  |  |  |  |  |  |  |  |  |

† Data not available for this birth cohort.

\*\*\* *p* *<0.05*

**

**Figure 2.** Historical context over the life course for cohorts born 1906-07, 1922, 1930, and 1944 in Sweden:

Adapted from Skoog I. Nature Reviews Neurology 12, 316-318 (2016) 51.

**Figure Legends**

**Figure 1.** One-month prevalence of major, minor and any depression by sex and examination year:

\*\*\* *< 0.05*

OR = Odds Ratio

**Figure 2.** Historical context over the life course for cohorts born 1906-07, 1922, 1930, and 1944 in Sweden:

Adapted from Skoog I. Nature Reviews Neurology 12, 316-318 (2016) 51.

**Supplementary Table 1.** The association† between mean neuroticism score‡ and depression by sex and examination year

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | | | | |  |  | | | | |  |  | | | | |
| Examination year | 1976-77 | | | | |  | 1992-93 | | | | |  | 2014-16 | | | | |
| Birth cohort | 1906-07 | | | | |  | 1922 | | | | |  | 1944 | | | | |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | **OR** | **SE** | **df** | ***p*** | **(95 % CI)** |  | **OR** | **SE** | **df** | ***p*** | **(95 % CI)** |  | **OR** | **SE** | **df** | ***p*** | **(95 % CI)** |
| **Any depression** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| All | 1.24 | 0.04 | 1 | *<0.01* | (1.15-1.34) |  | § | § | § | § | § |  | 1.33 | 0.03 | 1 | *<0.01* | (1.26-1.41) |
| Men | 1.17 | 0.08 | 1 | *0.035* | (1.01-1.36) |  | § | § | § | § | § |  | 1.34 | 0.04 | 1 | *<0.01* | (1.23-1.46) |
| Women | 1.26 | 0.05 | 1 | *<0.01* | (1.14-1.39) |  | 1.42 | 0.06 | 1 | *<0.01* | (1.25-1.61) |  | 1.32 | 0.04 | 1 | *<0.01* | (1.23-1.42) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Major depression** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| All | 1.36 | 0.07 | 1 | *<0.01* | (1.19-1.55) |  | § | § | § | § | § |  | 1.34 | 0.05 | 1 | *<0.01* | (1.23-1.47) |
| Men | 1.11 | 0.13 | 1 | *0.43* | (0.86-1.43) |  | § | § | § | § | § |  | 1.38 | 0.08 | 1 | *<0.01* | (1.19-1.59) |
| Women | 1.50 | 0.10 | 1 | *<0.01* | (1.22-1.83) |  | 1.39 | 0.08 | 1 | *<0.01* | (1.19-1.63) |  | 1.32 | 0.06 | 1 | *<0.01* | (1.18-1.48) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Minor depression** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| All | 1.15 | 0.04 | 1 | *0.01* | (1.05-1.25) |  | § | § | § | § | § |  | 1.27 | 0.03 | 1 | *<0.01* | (1.21-1.35) |
| Men | 1.19 | 0.09 | 1 | *0.05* | (1.00-1.41) |  | § | § | § | § | § |  | 1.27 | 0.04 | 1 | *<0.01* | (1.17-1.39) |
| Women | 1.12 | 0.05 | 1 | *0.03* | (1.01-1.24) |  | 1.27 | 0.06 | 1 | *<0.01* | (1.12-1.44) |  | 1.27 | 0.04 | 1 | *<0.01* | (1.18-1.36) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | **R2** | **B (SE)** | **df** | ***p*** | **(95 % CI)** |  | **R2** | **B (SE)** | **df** | ***p*** | **(95 % CI)** |  | **R2** | **B (SE)** | **df** | ***p*** | **(95 % CI)** |
| **MADRS score** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| All | 0.23 | 0.6 (0.06) | 1 | *<0.01* | (0.47-0.70) |  | § | § | § | § | § |  | 0.27 | 0.7 (0.03) | 1 | *<0.01* | (0.59-0.72) |
| Men | 0.09 | 0.3 (0.09) | 1 | *<0.01* | (0.16-0.51) |  | § | § | § | § | § |  | 0.27 | 0.6 (0.04) | 1 | *<0.01* | (0.53-0.71) |
| Women | 0.27 | 0.7 (0.09) | 1 | *<0.01* | (0.52-0.87) |  | 0.30 | 0.9 (0.10) | 1 | *<0.01* | (0.73-1.14) |  | 0.26 | 0.7 (0.05) | 1 | *<0.01* | (0.59-0.77) |

† GLM (independent variable=neuroticism)

‡ Mean neuroticism score was not available for the examination in 2000-02 (birth cohort 1930).

§ Data not available (only women were examined in 1992-93 (birth cohort 1922))