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

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

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Therese Rydberg Sterner1\*, Pia Gudmundsson1, Robert Sigström1, Felicia Ahlner1, Nazib Seidu1, Anna Zettergren1, Silke Kern1, Svante Östling1, Margda Waern1, Ingmar Skoog1

1Neuropsychiatric Epidemiology Unit, Department of Psychiatry and Neurochemistry, Institute of Neuroscience and Physiology, Sahlgrenska Academy, Centre for Ageing and Health (AGECAP) at the University of Gothenburg, Sweden.

**Corresponding author**

**\***Therese Rydberg Sterner: therese.rydberg.sterner@neuro.gu.se

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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.

As populations are ageing world-wide 6, most of the projected gains in life expectancy will occur among those above age 65 years 7, 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 8. However, age- and sex-specific projections are uncertain as the prevalence of depression may change over time 9. An increase in depression is suggested for younger 10, and middle-aged 11 populations. Among older adults the prevalence of major depression has been found to be stable 12, while milder forms of depression have been reported to increase 13, decrease 9 or fluctuate 14 over time. Studies also show inconclusive time trend results 15. Few studies have examined time trends beyond 2010.

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.

**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, we examined whether the personality trait neuroticism, which is strongly associated with depression, has changed over time.

**METHODS AND MATERIALS**

**Participants**

The participants originate from the Gothenburg H70 Birth Cohort Studies in Sweden (the H70 studies) 16. 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%) 17. 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%) 18. 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%). 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 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 13.

The psychiatric examination comprised ratings of psychiatric symptoms and signs experienced in the past month according to the Comprehensive Psychopathological Rating Scale (CPRS) 19, which has good reliability among older persons 20. Depressive symptom burden was rated according to the Montgomery-Åsberg Depression Rating Scale (MADRS) 21. 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 22.

**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 23. 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 symptom algorithms based on the CPRS, in accordance with previous analyses from the H70 studies 24. Major depression was diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) 25, and required the presence of at least 5 out of 9 pre-specified depressive symptom clusters, 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 26 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 only. 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 27. 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 28. The observed agreement between the two classification systems was high (K = 0.81) 29.

**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 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 30. 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**

Fisher's exact test 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. 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. 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)

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). Treatment rate for 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 treatment rate 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).

**Burden of depressive symptoms**

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

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.

(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. 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. 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.

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 3, 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. 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). 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.

(Insert Table 3)

There was a strong association between neuroticism and depression at all examinations. The odds ratio for having higher neuroticism score for those with depression ranged between 1.4:1, 1.4:1 and 1.3:1 (*p*<001) for major depression, 1.2:1, 1.3:1 and 1.3:1 (*p*<001) for minor depression, and 1.2:1, 1.4:1 and 1.3:1 (*p*<001) for any depression. The association was also strong between neuroticism and MADRS score (R2=0.26; *p*<0.001).

**Sex differences**

Table 4 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 4)

**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 2,31. However, the gender gap decreased over time.

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 32. 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 (see Supplementary Figure 1).

(Insert Supplementary Figure 1)

Still, due to cultural gender norms, women face a role strain overload 33, 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 34, 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. 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 35, or the presence of biological differences, e.g. related to hormonal or genetic factors. Our findings highlight the importance of environmental factors. This may also support the peak in the prevalence of depression noted for women in 1992-93, which may partly be due to the economic recession occurring in Sweden during that time. As only women were examined in 1992-93, we do not know if the peak was present also for men. Depression and neuroticism may be influenced by how life courses are embedded in societal and geographical contexts across historical times 36, not only for women. 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. This is also reflected by the increased life expectancy between 1976 (approximately 72 for men and 78 for women) and 2014 (approximately 80 for men and 84 for women) 37. Our findings should also be seen in the light of decreasing prevalence of late-life dementia 38,39, and increased cognitive function 40, lung function 41, cardiovascular health 42, and sexual activity 43 among Swedish older persons in later-born birth cohorts.

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. 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 5,9. 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 11. Studies on major depression among older persons conducted during the same period report stable prevalence 12,13,44. 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 10,11,14,34,45-48, but the prevalence is also reported to be stable over time 49,50.

We have previously reported an increase in the prevalence of minor depression among 75-year-olds between 1976–77 and 2005–06 13. 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) 51-53. 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 14. Few other studies have a time span of more than four decades 50,54,55, 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 50, and the Lundby Study conducted 1947-97 reported a decreasing incidence of depression in 1972-1997 compared to 1947-1972 55.

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 56,57, and may therefore be affected by similar birth cohort effects. In support of this, we found a strong association between neuroticism and depression, in line with previous studies 58. 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 59. It could be noted that neuroticism also decreased among persons without 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 60. Paralleling previous studies, we found that the majority of persons with depression were not using antidepressants 49,61,62. 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.

**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 63.

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, 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 |
| % of birth cohort (N) | 44.4 (174) | 46.6 (227) | 46.5 (542) |  | 55.6 (218) | 100.0 (226) | 53.4 (260) | 53.5 (624) |
|  | **%** (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) |
| **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) |
| **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) |
| 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) |
|  |  |  |  |  |  |  |  |  |

† 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 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 |
| N (men/women) | (174/218) | (†/226) | (227/260) | (542/624) |  | (11/33) | (†/41) | (21/44) | (36/68) |  | (163/185) | (†/185) | (206/216) | (506/556) |
| **MADRS score**‡ (mean) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| All | 4.8§ | † | 4.6§ | 4.0 |  | 16.5 | † | 15.1 | 15.4 |  | 3.3 | † | 3.1 | 2.9 |
| Men | 3.6 | † | 3.9 | 3.6 |  | 14.6 | † | 14.3 | 14.6 |  | 2.8 | † | 2.8 | 2.8 |
| Women | 5.8§ | 6.1§ | 5.4 | 4.4 |  | 17.1 | 17.8 | 15.5 | 15.8 |  | 3.8§ | 3.5 | 3.4 | 3.0 |

† Data not available for this birth cohort.

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

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

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| **TABLE 3**. Mean neuroticism score 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 |
| N (men/women) | (151/178) | (†/194) | † | (520/602) |  | (10/26) | (†/31) | † | (33/63) |  | (141/152) | (†/163) | † | (487/539) |
| **Neuroticism score** (mean) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| All | 7.8§ | † | † | 6.1 |  | 12.5 | † | † | 10.8 |  | 7.2§ | † | † | 5.6 |
| Men | 6.1 | † | † | 5.5 |  | 8.9 | † | † | 10.8 |  | 5.9§ | † | † | 5.1 |
| Women | 9.2‡§ | 7.7§ | † | 6.6 |  | 13.9§ | 12.1 | † | 10.8 |  | 8.4‡§ | 6.8 | † | 6.1 |

† Data not available for this birth cohort.

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

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

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| **TABLE 4**. 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 Legends**

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

\*\*\* *< 0.05*

OR = Odds Ratio

**Supplementary Figure 1.** 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).