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**Self-reported loneliness in adolescents and its associations with mental disorders in young adulthood**

Data was obtained from the Young in Norway longitudinal study, coupled with data from the Norwegian Prescription Database.

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Master's thesis in Medicine (MED-3950), June 2022

# 1 Preface

When writing the master's thesis in Medicine, I wanted to investigate social determinants of mental health. Therefore, I contacted professor and specialist in psychiatry, Jørgen G. Bramness. Bramness introduced me to the opportunity of working with a data material from the Young in Norway longitudinal study, which formed the basis of this study. Data from the study was coupled with data from the Norwegian Prescription Database. The purpose of this study was to investigate the association between loneliness in adolescents and later prescriptions of psychotropic drugs.

I would like to thank my supervisor, Jørgen G. Bramness, for guidance and constructive feedback throughout the process. Not only has the collaboration been useful in an educational context, but it has taught me to look at mental health from a new perspective. We have had several interesting conversations and I have gained new knowledge about the complexity and importance of mental health and mental disorders.

Furthermore, I would like to thank my co-supervisor and project manager for the Young in Norway longitudinal study, Tilmann von Soest, for making this project possible. He facilitated the data in this study, while undersigned performed all statistical analyzes. It has been a privilege to work with such comprehensive and interesting data.

Finally, I would like to thank my partner, Mathias Bøkestad, for always engaging in discussions regarding health and for motivating me throughout the process.

**Karianne Lotre**
Tromsø, 28.05.2022

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# 2 Abstract

**Objective**

Loneliness is particularly prevalent during adolescence and has been associated with unfortunate effects on both physical and mental health. In this longitudinal study, we investigate if loneliness in adolescents is associated with later prescriptions of antidepressants, antipsychotics, mood stabilizers and anxiolytics. Prescriptions of psychotropic drugs are used as an indirect measure of mental disorders.

**Methods**

Data on loneliness and potential confounders were obtained from 2602 individuals in the Young in Norway longitudinal study. Data was coupled with the Norwegian Prescription Database, with information about prescriptions of psychotropic drugs from 2007 to 2015.

**Results**

Loneliness among adolescents was prospectively associated with prescriptions of antidepressants (OR = 1.60, CI 95% 1.25-2.06, p = < 0.001) and antipsychotics (OR = 2.33, CI 95% 1.26-4.30, p = 0.007). No association was found between self-reported adolescent loneliness and later prescriptions of mood stabilizers or anxiolytics. Those not receiving prescriptions of psychotropic drugs, had parents with higher education, were more often living with both parents, had less conduct problems and mental distress.

**Conclusion**

In this longitudinal cohort study, self-reported loneliness in adolescents was associated with later prescriptions of antidepressants and antipsychotics, indicating that self-reported adolescent loneliness is associated with later depression and psychotic disorders, and perhaps anxiety. The findings in this study might provide valuable insight into how mental health in young adulthood can be influenced by social factors in adolescence. Loneliness is particularly prevalent in adolescents and has potential negative effects on mental health.

# 3 Introduction

Mental disorders are one of our major public health challenges (1). According to the Norwegian public health report (2), mental disorders were the fourth largest cause of overall burden of disease in Norway in 2019. Burden of disease encompasses how diseases, injuries and risk factors affect a population in form of health loss and mortality (3). Furthermore, the Norwegian government has developed a strategy for good mental health, proposing that we need more openness and knowledge about mental health (4).

Mental health is determined by multiple social, psychological, and biological factors (5). Some important environmental risk factors for mental disorders include biological factors (e.g., birth complications), problems in interpersonal relations (e.g., loneliness, social isolation, bullying) and family conditions (e.g., abuse, stressful life events, low socioeconomic status) (6). Furthermore, twin- and adoptions studies have shown that genetic factors are important for development of mental disorders (7). There is a high degree of heredity in schizophrenia and bipolar disorder, slightly less in severe depression and moderate in anxiety. However, the causes of mental disorders are complex, and knowledge of the exact causes is still deficient (6).

Regarding social determinants of mental health, one of the strategies proposed by the Norwegian government (4), is to strengthen social support and reduce loneliness. Good social support is considered important for mental health, and lack of social support will often be synonymous with loneliness. Although loneliness is a mild and transient experience for most people, for some people it can be more severe and prolonged, thus leading to harmful consequences for both physical and mental health (8). So far there is a growing body of literature on the unfortunate effects of loneliness on physical health (9-12). For instance, loneliness has shown to be predictive of coronary heart disease and stroke (9, 12), increased systolic blood pressure (10) and Alzheimer's disease (11). Furthermore, loneliness has been associated with higher mortality rates along with well-established risk factors such as smoking, obesity and physical inactivity (13-15). However, there is not much longitudinal evidence on loneliness and mental disorders (15), which formed the basis of this retrospective longitudinal study.

## 3.1 Mental disorders

The term mental disorder refers to a large variety of conditions and diagnoses, which are characterized by disturbances in thoughts, feelings, behavior and/or level of social functioning (2). The different disorders are classified according to international diagnostic criteria, that are revised regularly in accordance with updated scientific evidence. In this paper we are focusing on depression, anxiety disorders, bipolar disorder, and schizophrenia.

Mental disorders are widespread in the Norwegian population (6). It is estimated that 16-22% of the adult population will suffer from a mental disorder over a course of a year. Depression and anxiety disorders are among the most common disorders in both adolescents and adults. The prevalence of depressive disorders varies from 0.1-1.6% in pre-adolescent children and 2.2-3.2% when adding adolescents. The prevalence is higher among adolescent girls than boys, and the lifetime prevalence is estimated to 14.3%. In adults, about one in five will suffer from depression during their lifetime, and one in ten over a course of a year. Anxiety disorders are common in all ages, however, more prevalent in adolescents with a lifetime prevalence estimated to 31.9%. In adults, about one in four will suffer from an anxiety disorder during their lifetime, and about 15% during a course of a year. Psychotic disorders, where schizophrenia is the most common disorder, rarely occurs in adolescence. The lifetime prevalence of psychotic disorders in adults is estimated to about 1-3.5% (2). Bipolar disorder is also rare in children, but the occurrence has not been satisfactorily investigated (16). A Norwegian study found a lifetime-prevalence of bipolar disorder of 1.6% (6).

However, measuring occurrence of mental disorders has its challenges (6). Some studies report lifetime occurrence, while others report 12-month occurrence. The results also vary between studies. This is partly explained by different age composition in the study populations, differences in measuring and diagnostic instruments and difference in occurrence between countries. The numbers can still provide a picture of the occurrence but must be interpreted with caution.

## 3.2 Psychotropic drugs

Psychotropic drugs have a central place in the treatment of mental disorders, especially in more severe conditions (2). Non-pharmacological approaches such as psychotherapy, are also important, either alone or in combination with medications (17). Although not all mental

disorders are treated with medicinal drugs, the rate of drug treatment is however substantial, making it possible to use prescriptions for these drugs as an indirect measure of mental disorders. Our focus in this study is on antidepressants, antipsychotics, anxiolytics, and mood stabilizers.

### 3.2.1 Antidepressants

Antidepressants are used to treat depression and the most common drug is selective serotonin reuptake inhibitors (SSRIs; e.g. citalopram, fluoxetine, paroxetine and sertraline) (17, 18). Choice of treatment depends on symptoms and the severity of the depression (19). For instance, in mild and moderate depression, psychotherapy is often the first choice of treatment (17). The effect of antidepressants in children and adolescents is uncertain, and psychosocial interventions are often first line of treatment (18). Some antidepressants are also used on other indication than depression, for instance anxiety disorders and obsessive-compulsive disorder.

### 3.2.2 Antipsychotics

Antipsychotics are primarily used in the treatment and prevention of psychotic disorders, including schizophrenia (20). Some antipsychotics are also used in treatment of bipolar disorder. For instance, severe manic symptoms are usually treated with an antipsychotic drug in combination with lithium, carbamazepine, or valproate (21). According to the Norwegian public health report (2), the proportion of adults in the population treated with antipsychotics has been stable from 2010 to 2020.

### 3.2.3 Anxiolytics

Anxiolytics have anxiolytic, sedative, hypnotic, muscle relaxant and anticonvulsant effects (22). There is mainly difference in dosage that gives different effects. Earlier, benzodiazepines were used extensively in the treatment of anxiety (2). However, they are known to be addictive, and thus not recommended in long-term treatment. According to the latest guidelines they are now mostly limited to symptomatic treatment, for instance in short-term treatment of anxiety disorders, sleeping problems accompanied by anxiety or while waiting for other drug treatment to work (2, 22). Since 2010, there has been a steady decline in use of benzodiazepines in treatment of anxiety, which is considered a desired development and in relation to guidelines (2).

### 3.2.4 Mood stabilizers

The main groups of mood stabilizers are lithium and antiepileptics (17). Acute treatment of mania and depression in patients with bipolar disorder, as well as long-term prophylactic treatment, are the main indications for lithium (23). Antiepileptics (e.g., valproate, lamotrigine) are also used in bipolar disorder, but mostly to prevent depressive episodes (17). Other antiepileptics (e.g., phenytoin) are used to treat epilepsy (21).

## 3.3 Loneliness

Loneliness has been defined as a negative emotional state resulting from a discrepancy between desired and achieved social interaction or relationships (13, 24) It is a subjective experience of being socially isolated, in contrast to being alone (25). Of course, there is a relationship between real and perceived social interaction, but, people can live solitary lives without feeling lonely, while others can live a seemingly rich social life but still feel lonely (11). Studies investigating loneliness among adolescents, have found loneliness to be particularly prevalent during this time of life (26, 27). Adolescents undergo significant changes during the transition from childhood, regarding social expectations, relationships, roles and personal identities, which may influence loneliness (24).

Existing research on the effects of loneliness on mental health has shown that loneliness is associated with depression (24, 26, 28, 29), as well as anxiety disorders (11, 24, 27). People with difficulties in establishing and maintaining satisfying relationships with others, are likely to experience depression and anxiety (24). There is evidence that less perceived social support or greater loneliness at baseline is associated with higher depressive symptom severity, poorer recovery and worse functional outcomes at follow-ups (13). A study using longitudinal data on loneliness and depression among adults, found that interventions to reduce loneliness resulted in a reduction in depressive symptoms (29).

People with psychotic disorders frequently feel lonely (30), and studies suggest that loneliness may play a causal role in the development of psychotic experiences (30, 31). A systematic review conducted by Gayer-Anderson & Morgan (31), found that individuals having a first episode of psychosis, had smaller social networks compared to the general population. For instance, in a study with 224 cases with a first episode of psychosis and 322 controls, cases were three times more likely than controls to have a low frequency of contact with people in

their social network (32). Despite these findings, it is unclear whether loneliness precedes psychosis or occurs as a result of the condition (30).

A systematic review conducted by Wang et al. (13) investigated psychosocial variables among adults with bipolar disorder, and found that lower perceived social support was associated with greater depression, greater impairment in functioning and longer time to recovery. However, social support is conceptually distinct from loneliness (10). To our knowledge, little research exists on loneliness preceding bipolar disorder. A reason for this may be that the impact of loneliness on mental health outcomes still is insufficiently addressed (13).

Considering loneliness as risk factor for mental disorders seems reasonable. However, comparison of the association between loneliness and mental disorders is challenging. Some studies haven't adjusted for baseline measurements of outcomes (13), and most of the existing studies are cross-sectional, making it difficult to draw conclusions on direction of causality (15). In addition, several studies have investigated loneliness in people with a mental disorder, rather than loneliness preceding mental disorders (13, 33-35).

## 3.4  Aim

The aim of the present study was to investigate the association between loneliness in adolescents and mental disorders in young adulthood, measured by prescriptions of antidepressants, antipsychotics, anxiolytics, and mood stabilizers as proxy for mental disorders. We targeted adolescents since they are, as mentioned earlier, more prone to loneliness than others. We measured potential confounders at baseline, including age, gender, whether born in Norway, living with both parents, parental education, conduct problems and mental distress. Loneliness was assessed at four data collection waves, but our focus was on the first data collection wave as we wanted to investigate this age group.

## 3.5  Research question

To what extent is loneliness associated with later prescriptions of antidepressants, antipsychotics, anxiolytics, and mood stabilizers?

# 4 Methods

## 4.1 Study design and data material

This longitudinal cohort study was based on data from the Young in Norway longitudinal (YiN-long) study, a prospective cohort study providing survey data from four collection waves between 1992 and 2005 (table 1). YiN-long is Norway's first major longitudinal study of youth and is based on self-report questionnaires regarding multiple aspects of their lives, for instance education, network, personal development and mental health (36). Data from the YiN-long were linked to data on filled prescriptions from the Norwegian Prescription Database (NorPD), with special emphasis on prescriptions of antidepressants, antipsychotics, anxiolytics, and mood stabilizers. NorPD is administered by the Norwegian Institute of Public Health and monitors prescriptions prescribed to pharmacies outside of institutions to individuals (37).

**Table 1.** The data collection waves of the Young in Norway longitudinal (YiN-long) study.

| Data collection | Year | Response rate |
|---|---|---|
| 1. data collection wave ($T_1$) | 1992 | 97% |
| 2. data collection wave ($T_2$) | 1994 | 79% |
| 3. data collection wave ($T_3$) | 1999 | 68% |
| 4. data collection wave ($T_4$) | 2005 | 82% |

## 4.2 Procedure and participants

The YiN-long started in 1992 with a national sample composed of students from 67 junior and senior high schools in Norway, with each grade being equally represented (38). Every school in the country was included and the only exclusion criteria was severe lack of reading capability (39). About 12.000 students participated (36). The participants were followed up in 1994, and a subsample was further followed up in 1999 and 2005. The mean age of the participants across the four data collection waves were $T_1$: 15.1 (SD = 2.0 years), $T_2$: 16.5, $T_3$: 23.0 and $T_4$: 28.5 years. At the last data collection wave ($T_4$), respondents were asked for their consent to link the data to several registers, including NorPD. 2602 respondents consented and data in the present study was obtained from this sample, consisting of 1145 males (44%) and 1457 females (56%).

## 4.3 Variables

### 4.3.1 Sociodemographics

Gender, age, country of birth and whether respondents were living with both parents (yes/no) were assessed at $T_1$. We also asked about parental education, which was classified into five levels from 1 (*up to 9 years of basic education*) to 5 (*more than three years of university education*) for the parent with the highest education, as an indirect measure of socioeconomic status.

### 4.3.2 Relationship

At $T_4$, respondents were asked if they ever had a steady girlfriend/boyfriend or partner (no/yes). If the answer was yes, they were further asked about age, gender, and duration of relationship.

### 4.3.3 Conduct problems and smoking

A 15-item measure of conduct problems was assessed at $T_1$. The items are closely related to the diagnostic criteria for conduct disorder in the DSM-III-R (40). The respondents were asked if they ever have taken part or done specific actions during the last year, such as «have you broken in somewhere to steal something». Response options ranged from 1 (*never*) to 6 (*more than 50 times*). Smoking was assessed at $T_4$, with response options from 1 (*have never smoked*) to 5 (*smoke daily, about ... cigarettes*).

### 4.3.4 Mental health and previous prescriptions

Mental distress was measured at $T_1$ by a 12-item version of the Hopkins Symptom Checklist (HSCL). It is a self-report symptom inventory and is scored on five underlying symptom dimensions: somatization, obsessive-compulsive, interpersonal sensitivity, anxiety and depression (41). The scale has been used in a previously published paper based on data from YiN-long, and showed a satisfactory internal consistency (38). The measure used in YiN-long asks for rating of symptoms of depression and anxiety the preceding week. It applies a 4-point response scale: 1 (*not bothered at all*), 2 (*a little bit bothered*), 3 (*quite a bit bothered*) and 4 (*extremely bothered*). Mean scores were computed, and higher scores indicated higher levels of mental distress. Prescriptions of psychotropic drugs in 2004 was also carried out.

### 4.3.5 Loneliness

Loneliness is commonly assessed using the revised UCLA Loneliness Scale (UCLA-R), which consists of 20 items measuring a general degree of satisfaction with one's social relationships (35). The instrument has shown a high internal consistency. In this study we used a four-item short version of the scale, which is considered as an adequate substitute and is recommended in survey research (42). This version consists of two positively worded items assessing social loneliness («*I feel in tune with the people around me*» and «*I cand find companionship when I want it*») and two negatively worded items assessing emotional loneliness («*No one really knows me well*» and «*People are around me but not with me*»). In addition, as a direct measure of loneliness, a $5^{th}$ item *(«I feel lonely»)* has been included in the YiN-long study. Each item was answered on a 4-point response scale, that is, 1 (*never*), 2 (*rarely*), 3 (*sometimes*) and 4 (*often*). The positively worded items were reverse coded before the analysis, with higher scores indicating higher levels of loneliness (25).

## 4.4 Outcome

The outcome in this study was the use of psychotropic drugs as they appear as filled prescriptions in NorPD. Subjects were categorized according to their filling of prescription of psychotropic drugs, which were categorized according to anatomical-therapeutic-chemical (ATC) codes as receiving either antidepressants, antipsychotics, anxiolytics, or mood stabilizers. In addition, a fifth group, «psychotropic drugs on other indications», was made to account for those receiving medication on other indication than psychiatric disorders (for instance epilepsy). Data on filled prescriptions was collected during a nine-year period from 2007 to 2015.

The grouping of psychotropic drugs was performed according to hierarchical decision rules: (1) mood stabilizers, (2) antipsychotics, (3) antidepressants, (4) anxiolytics, and (5) psychotropic drugs on other indications. This was performed to account for persons who received medications from more than one category. For instance, if a person was described both mood stabilizers and antidepressants, the person was categorized as receiving mood stabilizers. The categorization was performed on the bases of an expert review of each prescription story of every subject. Some exceptions were made to account for only low-dose prescriptions and cases of only one prescription.

## 4.5   Statistical analyses

Statistical analyses were done using the statistical program SPSS. Descriptive statistics was carried out to characterize the sample at baseline (age, gender etc). Bivariate analyses were conducted by Pearson chi-square test with means of $\chi^2$ for categorical variables presented in rows, and prescription of psychotropic drugs presented in columns. For continuous variables, Analysis of Variance (ANOVA) with means and standard deviation was carried out, with prescription of psychotropic drugs as independent variable.

Further bivariate analyses were carried out to investigate associations between background variables (e.g., sociodemographics, mental health) and UCLA loneliness mean score at $T_1$. All continuous variables were recoded into categorical variables (for example age $\leq 14$ years and $> 14$ years). Difference test was conducted by ANOVA with UCLA loneliness mean score at $T_1$ as dependent variable.

The association between loneliness at baseline and later prescriptions of psychotropic drugs was tested using multinomial logistic regression. Only statistically significant variables from bivariate analyses were included in the regression analyse. For all analyses, a $p$ value of $< 0.05$ was considered statistically significant. The regression analyses were conducted using prescriptions of psychotropic drugs as dependent variable and UCLA loneliness mean score at $T_1$ as the independent variable. The different categories of psychotropic drugs were compared to the reference category «no psychotropic drugs». Adjustment for potential confounders were done in five steps by first including age and gender. We then adjusted for all sociodemographic variables at baseline (age, gender, origin, parental education and living with both parents), to test whether the observed association was independent of all sociodemographic variables. We adjusted for conduct problems and smoking as a third step, and mental distress in a fourth step. Finally, we added prescriptions of psychotropic drugs in 2004 to adjust for those receiving medication before data on filled prescriptions from NorPD was collected. Categorical variables were computed as factors, whereas continuous variables were computed as covariates.

## 4.6   Ethical considerations

The Young in Norway longitudinal study (YiN-long) is approved by The Privacy Ombudsman at Oslo Metropolitan University and by the Regional Committees for Medical

and Health Research Ethics South-East A (REK South-East A, reference 25462) (43). The participants in the study have completed several self-report questionnaires and the answers have been treated confidentially, with information being processed without name, birth number or other directly recognizable information. Each participant has a code that links information through a list of names, and this is stored in a secure way at the Norwegian Center for Research Data (NSD). In addition, the participants were asked to link questionnaire data to data from several administrative registers, and this has only been done for the participants who consented.

## 4.7   Access to data

Data was made available through a file that is stored on a safe computer at University of Oslo. Co-supervisor and project manager of the YiN-long study, Tilmann von Soest, applied for and received approval for the project from the Regional Committees for Medical and Health Research Ethics (REK) (reference: 25462).

# 5 Results

## 5.1 Descriptive summary

The total sample of 2602 individuals consisted of 1145 males (44%) and 1457 females (56%). The mean age of the participants was 15.2 at $T_1$. Most of the participants were born in Norway and were living with both parents. Data on loneliness was missing for 209 participants at $T_1$, 124 at $T_2$, 298 at $T_3$ and 1 participant at $T_4$. During the 9-year follow up period, 233 respondents (9.0%) were categorized as receiving antidepressants, 33 (1.3%) received antipsychotics, 102 (3.9%) used anxiolytics, 36 (1.4%) received mood stabilizers, and 84 (3.2%) used psychotropic drugs on other indication. Most of the population had not received prescriptions of psychotropic drugs (n= 2114, 81.2%).

## 5.2 Potential confounders

### 5.2.1 Sociodemographics

There were differences between the prescription categories on all variables except age and being born in Norway (table 1). Those who were not prescribed any psychotropic drugs were more often living with both parents and had parents with higher education, compared to those with prescription of psychotropic drugs. All prescription categories, except for antipsychotics, had highest proportion of women. Lowest level of parental education was found among respondents later receiving antipsychotics.

### 5.2.2 Conduct problems and smoking

Participants not using psychotropic drugs had less conduct problems and lowest proportion of daily smokers, compared to those receiving psychotropic drugs (table 1). Participants later using anxiolytics had highest score of conduct problems, while respondents in the mood stabilizers category reported highest level of daily smoking.

### 5.2.3 Mental health and previous prescriptions

Highest mean score of mental distress was found among those later receiving antidepressants, while lowest score was found among those who did not get any prescription (table 1). Highest proportion of psychotropic drug prescription in 2004 was reported among participants later receiving prescription of mood stabilizers.

**Table 1.** Loneliness, sociodemographics, conduct problems, smoking and mental health according to filling prescriptions for psychotropic drugs

| | | No psychotropic drugs | Antipsychotics | Mood stabilizers | Antidepressants | Anxiolytics | Psychotropic drugs on other indications | Difference test[a] | |
|---|---|---|---|---|---|---|---|---|---|
| | | n = 2114 (81.2%) | n = 33 (1.3%) | n = 36 (1.4%) | n = 233 (9.0%) | n = 102 (3.9%) | n = 84 (3.2%) | $\chi^2$ / F | p-value |
| **Loneliness** | | | | | | | | | |
| UCLA loneliness scale ($T_1$) | mean (SD) | 1.84 (0.53) | 2.11 (0.45) | 1.86 (0.62) | 1.98 (0.59) | 1.81 (0.55) | 1.98 (0.50) | 4.99 | < 0.001 |
| UCLA loneliness scale ($T_2$) | mean (SD) | 1.80 (0.55) | 1.84 (0.56) | 1.79 (0.60) | 1.96 (0.62) | 1.71 (0.48) | 1.83 (0.57) | 4.05 | 0.001 |
| UCLA loneliness scale ($T_3$) | mean (SD) | 1.80 (0.49) | 2.01 (0.49) | 1.97 (0.46) | 1.99 (0.54) | 1.82 (0.56) | 1.77 (0.47) | 8.65 | < 0.001 |
| UCLA loneliness scale ($T_4$) | mean (SD) | 1.74 (0.47) | 2.30 (0.63) | 2.19 (0.55) | 2.01 (0.56) | 1.78 (0.54) | 1.76 (0.50) | 26.01 | < 0.001 |
| **Relationship** | | | | | | | | | |
| Girlfriend/boyfriend/partner ($T_4$) | n (%) | 1997 (95.0) | 30 (90.9) | 34 (94.4) | 215 (92.7) | 98 (98.0) | 80 (95.2) | 5.39 | 0.370 |
| **Sociodemographics** | | | | | | | | | |
| Female gender ($T_1$) | n (%) | 1137 (53.8) | 15 (45.5) | 25 (69.4) | 154 (66.1) | 69 (67.6) | 57 (67.9) | 28.39 | < 0.001 |
| Age ($T_1$) | mean (SD) | 15.23 (1.87) | 14.88 (3.18) | 15.14 (3.18) | 15.28 (2.15) | 15.37 (1.92) | 15.37 (2.41) | 0.43 | 0.828 |
| Born in Norway ($T_1$) | n (%) | 1,925 (97.0) | 27 (93.1) | 32 (94.1) | 214 (96.8) | 94 (96.9) | 77 (98.7) | 3.27 | 0.659 |
| Parental education ($T_1$) | mean (SD) | 3.42 (1.12) | 3.08 (1.13) | 3.33 (1.18) | 3.16 (1.07) | 3.33 (1.12) | 3.21 (1.10) | 2.60 | 0.024 |
| Living with both parents ($T_1$) | n (%) | 1450 (71.5) | 20 (64.5) | 24 (70.6) | 130 (57.5) | 56 (55.4) | 56 (70.0) | 28.74 | < 0.001 |
| **Conduct problems and smoking** | | | | | | | | | |
| Conduct problems ($T_1$) | mean (SD) | 1.34 (0.37) | 1.36 (0.35) | 1.37 (0.46) | 1.41 (0.40) | 1.45 (0.53) | 1.41 (0.45) | 2.71 | 0.019 |
| Daily smoking ($T_4$) | n (%) | 358 (17.0) | 17 (51.5) | 19 (52.8) | 74 (31.9) | 30 (29.7) | 19 (22.9) | 117.80 | < 0.001 |
| **Mental health and previous prescriptions** | | | | | | | | | |
| Mental distress ($T_1$) | mean (SD) | 1.57 (0.45) | 1.70 (0.55) | 1.65 (0.48) | 1.80 (0.53) | 1.64 (0.43) | 1.65 (0.46) | 10.75 | < 0.001 |
| Psychotropic drug prescription in 2004 | n (%) | 40 (1.9) | 12 (36.4) | 19 (52.8) | 42 (18.0) | 10 (9.8) | 11 (13.1) | 373.40 | < 0.001 |

[a]Difference tests conducted by means of $\chi^2$ (categorical variables) and analysis of variance (ANOVA) (continuous variables) statistics.

## 5.3   Loneliness and prescriptions of psychotropic drugs

Descriptive statistics showed that highest mean score of loneliness was reported among those later receiving antipsychotics in all data collection waves, except for $T_2$, where highest mean score was among those using antidepressants (table 1, figure 1). Lowest mean score was found among respondents using anxiolytics ($T_1$, $T_2$) psychotropic drugs on other indication ($T_3$) and those who did not receive any prescription ($T_4$). There were no differences between the prescription categories and having a girlfriend, boyfriend, or partner.

**Figure 1.** The UCLA-loneliness mean score at $T_1$-$T_4$ according to filling prescriptions of psychotropic drugs
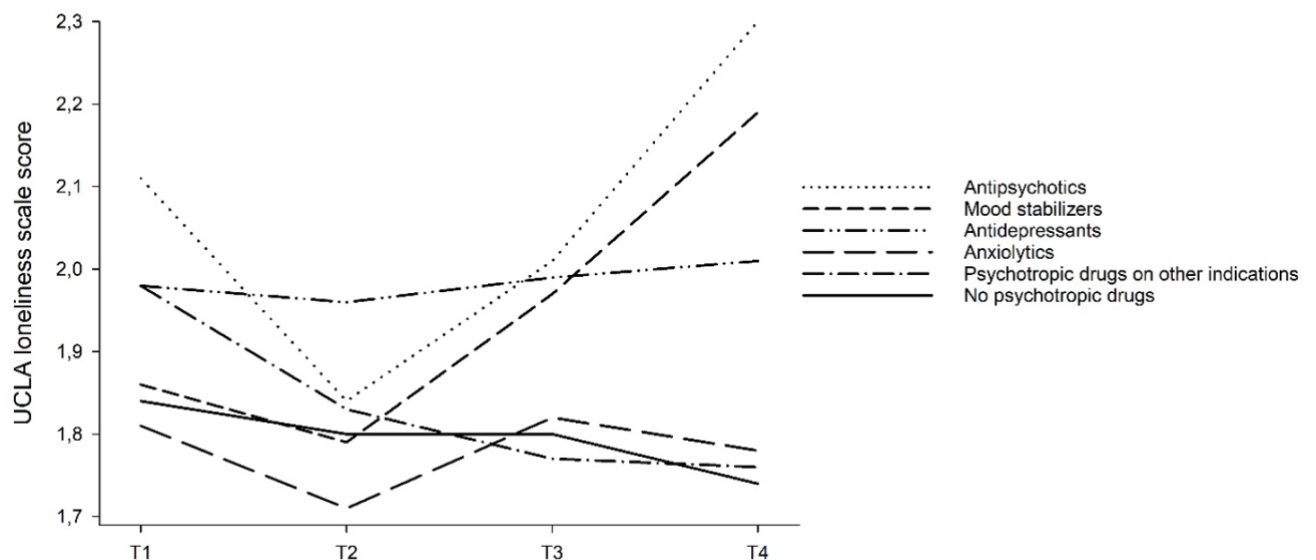


All sociodemographic variables, except living with both parents, were statistically significant according to UCLA loneliness mean score at $T_1$ (table 2). Higher mean score of loneliness was reported among respondents $\leq 14$ years, who had other origin than Norway, and who had parents with lower level of education. Respondents with high mental distress and previous prescription of psychotropic drugs, had higher mean score of loneliness compared to those with low mental distress and no previous prescription. No significant association was seen between loneliness and conduct problems ($p = 0.497$) or daily smoking ($p = 0.334$).

**Table 2.** Sociodemographics, conduct problems, smoking, mental health, and previous prescriptions according to UCLA-loneliness mean score (SD) at $T_1$

| | | UCLA loneliness scale $T_1$ | Difference test[a] | |
|---|---|---|---|---|
| | | Mean score (SD) | F | p-value |
| **Sociodemographics** | | | | |
| Gender ($T_1$) | Female | 1.88 (0.54) | 4.86 | 0.028 |
| | Male | 1.83 (0.53) | | |
| Age ($T_1$) | ≤ 14 years | 1.88 (0.54) | 3.70 | 0.054 |
| | > 14 years | 1.84 (0.52) | | |
| Born in Norway ($T_1$) | Yes | 1.85 (0.53) | 7.53 | 0.006 |
| | No | 2.03 (0.63) | | |
| Parental education ($T_1$) | Below higher education | 1.87 (0.54) | 4.77 | 0.029 |
| | Higher education | 1.82 (0.53) | | |
| Living with both parents ($T_1$) | Yes | 1.85 (0.53) | 3.28 | 0.070 |
| | No | 1.89 (0.55) | | |
| **Conduct problems and smoking** | | | | |
| Conduct problems ($T_1$) | Below cut-off (≤ 1.85) | 1.85 (0.54) | 0.46 | 0.497 |
| | Over cut-off (> 1.85) | 1.87 (0.53) | | |
| Daily smoking ($T_4$) | Daily smoker | 1.88 (0.56) | 0.93 | 0.334 |
| | Not daily smoker | 1.86 (0.53) | | |
| **Mental health and previous prescriptions** | | | | |
| Mental distress ($T_1$) | Below cut-off (≤ 1.85) | 1.77 (0.49) | 269.20 | < 0.001 |
| | Over cut-off (> 1.85) | 2.18 (0.56) | | |
| Psychotropic drug prescription in 2004 | Yes | 1.97 (0.56) | 4.98 | 0.026 |
| | No | 1.86 (0.53) | | |

[a]Difference test conducted by analysis of variance (ANOVA) (continuous variables)

The unadjusted results of the multinomial regression analyses showed a significant association between loneliness at $T_1$ and later prescriptions of antidepressants (OR = 1.60, CI 95% 1.25-2.06, p = < 0.001) and antipsychotics (OR = 2.33, CI 95% 1.26-4.30, p = 0.007). The association remained significant through three steps of adjustment, but with lower significancy compared to the baseline model and model one (table 3). Loneliness was also associated with prescriptions of drugs on other indications, but only through one step of adjustment (OR = 1.56, CI 95% 1.04-2.36, p = 0.033). No association was found between loneliness and later prescriptions of mood stabilizers or anxiolytics in any model.

**Table 3.** The impact of the total score of UCLA loneliness scale ($T_1$) on the prescriptions of psychotropic drugs. A multinomial logistic regression analyses.

| | Adjustment | Antipsychotics | | Mood stabilizers | | Antidepressants | | Anxiolytics | | Psychotropic drugs on other indications | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | OR (95% CI) | p-value | OR (95% CI) | p-value | OR (95% CI) | p-value | OR (95% CI) | p-value | OR (95% CI) | p-value |
| Baseline model | Unadjusted associations | 2.33 (1.26-4.30) | **0.007** | 1.06 (0.56-2.03) | 0.850 | 1.60 (1.25-2.06) | **< 0.001** | 0.88 (0.59-1.31) | 0.537 | 1.59 (1.05-2.40) | **0.027** |
| Model 1 | Adjustment for age and gender | 2.35 (1.27-4.35) | **0.007** | 1.04 (0.54-1.99) | 0.907 | 1.58 (1.22-2.03) | **< 0.001** | 0.86 (0.58-1.28) | 0.465 | 1.56 (1.04-2.36) | **0.033** |
| Model 2 | Additional for all socio-demographics [a] | 2.50 (1.24-5.03) | **0.010** | 1.29 (0.64-2.63) | 0.478 | 1.55 (1.18-2.04) | **0.002** | 0.86 (0.56-1.31) | 0.472 | 1.30 (0.82-2.06) | 0.258 |
| Model 3 | Additional for conduct problems and smoking | 2.41 (1.17-4.95) | **0.017** | 1.21 (0.58-2.49) | 0.610 | 1.51 (1.14-2.00) | **0.004** | 0.83 (0.54-1.27) | 0.390 | 1.36 (0.85-2.15) | 0.195 |
| Model 4 | Additional for mental distress | 2.19 (0.98-4.88) | 0.055 | 1.18 (0.53-2.64) | 0.685 | 1.23 (0.90-1.69) | 0.199 | 0.77 (0.48-1.24) | 0.276 | 1.29 (0.77-2.16) | 0.337 |
| Model 5 | Additional for use of psychotropic drugs in 2004 | 2.07 (0.89-4.82) | 0.092 | 1.16 (0.49-2.74) | 0.732 | 1.21 (0.88-1.68) | 0.243 | 0.76 (0.47-1.23) | 0.267 | 1.28 (0.76-2.15) | 0.349 |

Reference category: no psychotropic drugs. Statistically significant values are highlighted in bold.

OR = odds ratio; 95% CI = 95% confidence interval of OR.

[a] Born in Norway ($T_1$), Parental education ($T_1$) and Living with both parents ($T_1$)

# 6 Discussion

In this longitudinal cohort study of a population-based sample of adolescents, we found that self-reported loneliness in adolescents was prospectively associated with depression, psychotic disorders and perhaps anxiety in young adulthood, as measured by prescriptions of antidepressants and antipsychotics. These associations remained significant after adjusting for sociodemographic variables, conduct problems and smoking. No association was found between self-reported loneliness and later prescriptions of mood stabilizers or anxiolytics. Those not receiving prescriptions of psychotropic drugs, had parents with higher education, were more often living with both parents, had less conduct problems and mental distress.

## 6.1 Antidepressants

The association between loneliness and prescription of antidepressants is consistent with previous research about the relationship between loneliness and depression (24, 26, 28, 29). According to Heinrich & Gullone (24), several studies have found an association between loneliness and depression in both adolescents and adults. For instance, a study of college students found that loneliness at the start of a semester was predictive of depression later in the semester. However, some argue that loneliness and depression are overlapping conditions (24, 26). Indeed, in our study we found that those later receiving antidepressants, reported highest level of mental distress and second highest mean score of loneliness at baseline. These persons might have had depressive symptoms and maybe even depression at baseline, which exemplifies the challenge of determining cause or effect. Matthews et al. (26) suggest that the association between loneliness and depression may reflect common underlying genetic or environmental influences, which can contribute to the co-occurrence of loneliness and depression. In contrast, other analyses have shown that loneliness predicted increases in depression over one-year intervals, whereas depressive symptoms did not predict increases in loneliness (28). Furthermore, loneliness and depression are found to be associated with other individual characteristics, such as objective social isolation and low social support. Thus, these characteristics may act as a third variable, questioning the existence of a direct association between loneliness and depression.

## 6.2 Antipsychotics

We found a smaller but significant association between loneliness and prescription of antipsychotics. In addition, highest mean score of loneliness at $T_1$ was reported among those

later receiving antipsychotics. It is known that patients with psychosis experience a higher level of loneliness compared to the general population (8). Some studies also suggest that loneliness and reduced social networks might mediate the development of psychotic symptoms (8, 30, 31). One study investigating loneliness and psychotic symptoms found an association between loneliness and sub-clinical psychosis (e.g., at-risk mental state, psychotic-like experiences, or psychosis proneness) (8). Another study found that individuals experiencing a first episode of psychosis, had reduced social networks and social support (31). Poor premorbid social functioning has been strongly associated with smaller networks and number of friends, which may influence loneliness. It has also been suggested that one of the pathways leading to psychosis might be via poor self-concept and self-esteem (30). It would be reasonable to assume that loneliness may have a negative impact on self-concept and self-esteem, thus leading to psychosis. This suggest that loneliness may be a mediator in psychosis, rather than a direct cause.

However, it should be noted that findings from previous studies must be interpreted with caution, as they were mostly based on cross-sectional studies, which makes it difficult to establish the direction of causation (30, 31). Although this was a longitudinal study, the association we found may also be explained by confounders not included in this study. For instance, studies have found that cannabis use increases the risk of developing schizophrenia and psychotic symptoms (39). Furthermore, we only adjusted for symptoms of depression and anxiety at baseline, not other symptoms, or specific mental disorders. Therefore, we cannot rule out that participants had symptoms of psychotic disorders, or even an established diagnosis at baseline, suggesting that loneliness might be a consequence rather than a cause of psychotic disorders.

## 6.3 Anxiolytics

Some previous studies have found an association between loneliness and anxiety (11, 24, 27). However, we did not find an association between loneliness and prescription of anxiolytics in the present study. This might not be surprising, given that anxiolytics, in particular benzodiazepines, are mostly used in short-term treatment of anxiety disorders. In addition, anxiety disorders are often treated with antidepressants. Anxiety disorders, especially generalized anxiety, are also related to depression (44). It is therefore possible that there is an

association between loneliness and anxiety, but that these participants are treated with antidepressants and not anxiolytics.

## 6.4 Mood stabilizers

To our knowledge, existing literature on the relationship between loneliness and bipolar disorder is scarce. In this study, we did not find an association between loneliness and prescription of mood stabilizers. One study investigating psychosocial factors among adults found that lower perceived social support was associated with greater depression, greater impairment in functioning and longer time to recovery (13). However, the study was conducted among people already having bipolar disorder. It seems that social relationships are related to bipolar disorder, but there is a lack of evidence to distinguish cause and effect (13).

## 6.5 No psychotropic drug prescription

Most of the participants (81.2%) in this study did not receive prescriptions of psychotropic drugs. These persons had parents with higher education, were more often living with both parents, had less conduct problems and mental distress at baseline. This finding suggests that persons from a more protective background are at lower risk for developing mental disorders. Indeed, low socioeconomic status has been associated with mental disorders. As proposed by von Soest & Luhmann (25), parental economic position often shapes children's loneliness. It is reasonable that socioeconomic status matters for adolescents because it can provide more opportunities to participate in activities and engage with other adolescents, which in turn might decrease the possibility of loneliness.

## 6.6 Summary of findings

In summary, it seems reasonable to consider loneliness as a risk factor for mental disorders. As previous mentioned, loneliness occurs when there is a discrepancy between desired and achieved social interaction or relationships. Satisfying social relationships are considered vital for good mental health (24). When people fail to establish and maintain satisfying social relationships, they may experience feelings of depression, anxiety, loneliness, and anger. Lonely people also seem to be less satisfied with their lives. Indeed, problems in interpersonal relations have found to increase the risk of mental disorders. However, the causes of mental disorders are complex. Even though observations between environmental factors and mental disorders can be found, it is difficult to determine the causal relationship (6). Findings in this

study indicate that people with certain mental disorders in young adulthood report higher level of loneliness in adolescence and this may provide valuable insights into how social factors in adolescence can influence mental health later in life.

## 6.7   Methodological considerations

### 6.7.1   UCLA Loneliness Scale

To measure loneliness, we used the UCLA Loneliness Scale. The instrument has been extensively used in previous studies (25, 26, 35) and has shown a high internal consistency (45). However, it has some limitations. Firstly, we used the short version of the scale, with only four items to assess loneliness. A longer version of the scale would have increased the reliability (25). Second, we included a direct measure of loneliness *(«I feel lonely»)*. Direct measures have been criticized because people don't necessarily admit to feeling lonely given the social stigma attached to loneliness (25), which might lead to underreporting of loneliness. Third, loneliness was assessed solely by self-reporting questionnaires, which may be biased through shared method variance (24, 25). Finally, it is argued that the scale is a measure of long-term loneliness rather than short-term loneliness (24, 34), which makes it difficult to discriminate between consequences of chronic and situational loneliness (24). However, with prescription of psychotropic drugs as outcome in the present study, it seems reasonable to measure chronic rather than situational loneliness, given that chronic loneliness has the potential to impact mental health.

### 6.7.2   Prescriptions of psychotropic drugs

The outcome of this study was prescriptions of psychotropic drugs, which has been used in previous studies (39, 46). Prescriptions of psychotropic drugs can be used as an indirect measure of mental disorders, having knowledge about which drugs that are used to treat different disorders (6). However, we are not sure how well this outcome function as a measure of a specific mental disorder. For instance, antidepressants are used to treat both depression and anxiety disorders, and benzodiazepines are only recommended in short-term treatment of anxiety disorders. Thus, use of antidepressants and anxiolytics might be less valid as indirect measures of mental disorders. In addition, some people might receive non-pharmacological treatment for their mental disorder. In summary, prescriptions of psychotropic drugs might be quite specific for mental disorders, but not necessarily sensitive.

### 6.7.3 Sample size

The sample consisted of 2602 participants, however, most of the participants (n = 2114) did not receive prescription of psychotropic drugs. In principle, a larger sample size would be more representative because it would contain a larger part of the population (47). For instance, the effect size for the association between loneliness and antipsychotics (OR = 2.33) was greater than for antidepressants (OR = 1.60) in the baseline model. The trend continued when adjusting for several variables. However, the association between loneliness and antidepressants was more statistically significant (p = < 0.001) compared to antipsychotics (p = 0.007). This can be explained by the sample size in the different psychotropic drug categories. Antipsychotic users consisted of only 33 persons, whereas antidepressant users consisted of 233 persons.

## 6.8 Limitations and strengths

There are some limitations in this study itself. First, the sample used in this study were mainly Norwegian adolescents. Studies have found that persons in Northern European countries (including Norway) report lower levels of loneliness, compared to other European countries (25). This suggest that economic and cultural conditions may play a role, limiting the external validity of this study. Second, information on loneliness was measured in 1992 ($T_1$), whereas information on prescription of drugs was collected between 2007 and 2015. Changes in loneliness during this period might have affected the outcome. Indeed, participants using antipsychotics, reported higher mean score of loneliness at $T_4$ compared to $T_1$. Therefore, loneliness in adulthood might also explain the association found in this study. Third, we adjusted for several potential confounders at baseline, including age, gender, country of birth, whether living with both parents, parental education, and conduct problems. However, the observed associations might be explained by confounders not assessed in this study. In addition, we adjusted for mental distress at baseline by using the Hopkins Symptom Checklist. This instrument only asks for symptoms of anxiety and depression, not other symptoms, or specific diagnoses. This can result in participants having other symptoms of mental disorders, or even an established diagnosis at baseline. We did however adjust for psychotropic drug prescription in 2004, but participants might have received prescriptions prior to his. Finally, we did not conduct a strict, systematic literature search on loneliness and mental disorders. Thus, it may exist more relevant literature that would add valuable information regarding these matters.

One strength of the current study is the longitudinal design, allowing us to comment on the direction of causation, although conclusions about causality cannot be drawn. Second, the data material itself is unique due to the large number of participants, the high response rate, and the long follow-up time (36). Third, the study consisted of a large population-based sample of adolescents, providing valuable information about Norwegian adolescents. Participants from all junior and senior high schools in Norway were included, making the sample national representative. Fourth, we included several relevant confounders that could explain the observed association. Finally, the current study expands the knowledge of loneliness and its potential negative effects on mental health.

# 7 Conclusion

In this longitudinal cohort study, we found that self-reported loneliness in adolescents was prospectively associated with later prescriptions of antidepressants and antipsychotics, indicating that self-reported loneliness is associated with later depression and psychotic disorders, and perhaps anxiety. No association was found between self-reported loneliness and later prescriptions of mood stabilizers or anxiolytics. Those not receiving prescriptions of psychotropic drugs, came from a more protective background, suggesting that these persons might be at lower risk for developing mental disorders.

Although conclusions about causality cannot be drawn based on observational data, the results indicate that those having certain mental disorders in young adulthood reports higher level of loneliness in adolescence. The findings in this study might provide valuable insight into how mental health in young adulthood can be influenced by social factors in adolescence. Loneliness is particularly prevalent in adolescents and has potential negative effects on mental health.

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