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Anxiety problems in children: a population-based cohort study on incidence and management

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Abstract

Background: Due to a large strain on youth mental healthcare, general practice is suggested as an alternative treatment setting for children with anxiety problems. However, research on the current management of these children within general practice is scarce.

Aims: To investigate 1) the incidence of coded anxiety in general practice using the International Classification of Primary Care (ICPC) and 2) general practitioners’ (GPs) management of children presenting with anxiety problems.

Design and setting: Population-based cohort study using electronic medical records of 51,212 children (<18 years) in the Rotterdam region between 2012-2018.

Methods: First, the incidence of ICPC codes for anxiety was calculated. Second, characteristics of children consulting their GP with anxiety problems and the GPs’ management were assessed qualitatively using quantitative content analysis.

Results: The incidence of ICPC codes for anxiety in children was 5.36 per 1000 persons-years. Adolescent girls had the highest incidence with 14.01 per 1000 persons-years. Of the 381 children consulting their GP with an initial anxiety problem (median age: 13.3 years, 40.4% male), GPs referred 59.3% to mental healthcare in the first year and 26.5% of children were managed by a specialised practice nurse within general practice. 10.5% of children received psychiatric medication during the first year, with the trend being for increased prescriptions during adolescence.

Conclusion: In general practice children frequently receive one out of two ICPC codes for anxiety, especially adolescent girls. Most children presenting to their GP with anxiety problems are referred externally or seen by a specialised practice nurse within general practice.

Keywords:
Adolescents, anxiety, children, incidence, general practice, treatment

How this fits in?

Whilst general practice has been promoted for treating children with anxiety problems, little information on the actual treatment of these problems in general practice is available. This study shows that children in general practice in the Netherlands frequently receive an ICPC code for anxiety. The majority of children consulting their GP with a first anxiety problem are referred to mental healthcare. A quarter of these children are seen within general practice by a specialized practice nurse.
Introduction

Anxiety disorders form the most common mental health problem in children and adolescents and cause significant burdens. (1) A recent meta-analysis estimated the global prevalence of anxiety disorders among children and adolescents at 6.5%. (2) Anxiety disorders have significant negative effects on quality of life and the overall development of affected children and their next of kin, (3-6) and are associated with an increased risk of suffering from mental health disorders in adulthood. (7-10)

Despite the existence of effective treatments, (11-13) paediatric anxiety disorders seem underrecognized and undertreated. (14-20) Factors like stigmatization, financial costs, or limited access to services (e.g. waiting-lists) form major barriers to appropriate care. (21) General practice has been advocated as an appropriate treatment setting for paediatric mental health problems, because it is easily accessible and not associated with stigmatization. (22) GPs already play an important role in the help-seeking process to care, being a familiar and trusted source of help for children and parents. (23-25) In the Netherlands GPs have a gate-keeper role. GPs’ care is covered by health insurances, which are compulsory for all. During the past years in pilot-projects, youth mental health practice nurses (YMHPNs) have been introduced in Dutch general practice aiming to integrate mental health care into general practice. YMHPNs are involved in managing and referring children with psycho-social problems. (26, 27) YMHPNs work independently under the responsibility of GPs, and are allotted more time per consultation.

Several studies on the prevalence of paediatric anxiety disorders have been published, (2, 6, 28-33) but there is sparse knowledge on the incidence of paediatric anxiety symptoms and disorders in general practice. (34, 35) Little is known about how GPs actually manage these problems. In a UK survey, 51% of GPs felt confident identifying anxiety disorders in children, but only 13% felt confident managing them. (36) More information on how GPs currently manage anxiety problems in children is needed.

We, therefore, conducted two analyses: Firstly, we calculated the incidence of International Classification of Primary Care (ICPC) coded anxiety (P01 or P74) amongst children. Secondly, we used a broader sample of children with anxiety problems to describe the characteristics of children presenting to their GP, and the GPs’ management of these problems using qualitative analyses.

Methods

Design
We performed a population-based retrospective cohort study of children (0-17 years) registered in the Rijnmond Primary Care Database (RPCD) between January 1\(^{st}\) 2012 and December 31\(^{st}\) 2018.

The RPCD is a region-specific derivative of the Integrated Primary Care Information (IPCI) database, focused on the greater Rotterdam area.\(^{37, 38}\) RPCD contains pseudonymised longitudinal medical data of general practice patients, including complete GPs’ notes, diagnostic codes, referrals, laboratory findings, GPs’ prescriptions and specialists’ letters.\(^ {37} \) Dutch GPs use the International Classification for Primary Care 1 (ICPC-1) to code symptoms and diagnosis.\(^ {39} \) The RPCD currently contains data of approximately 300,000 primary care patients of more than 100 GPs.

**Incidence of ICPC coded anxiety (P01/P74) (quantitative analyses)**

We calculated the incidence of ICPC coded anxiety: P01 (feeling anxious/nervous/tense) or P74 (anxiety disorder/panic disorder), see Figure 1 Flowchart. For pragmatic reasons, we combined the codes P01/P74 for incidence calculation because the codes were used interchangeably by GPs in our database. The following characteristics of children receiving a first ICPC code P01/P74 were extracted from the database: date of coding, age, and sex.

**Case selection (qualitative analyses)**

Since paediatric anxiety problems in general practice often reflect symptoms rather than strict diagnostic categories, we were interested in children presenting with anxiety problems to their GP. Therefore, selected cases do not necessarily fulfil the diagnostic criteria of anxiety disorders but are rather a broader range of anxiety problems (e.g. anxiety problems of short duration).\(^ {40} \) We selected children presenting with a first anxiety problem to their GP (Figure 1: Flowchart, supplementary table S4). To increase the sensitivity for detecting children with anxiety problems, we used a search-algorithm combining ICPC codes P01/P74, ICPC code P02 (acute stress reaction/post-traumatic stress syndrome) and a free-text search for the terms ‘anxiety disorder’ and ‘anxiety problems’. To make valid inferences on the run-up period and GPs’ management, we limited inclusion to children with valid database information from two years before until two years after the first record of their anxiety problem. Full medical files from this period (600 cases) were examined by the principal investigator (LK) to exclude cases not registering an initial anxiety problem (Supplementary table S4). Unclear cases were reviewed by a senior researcher (ES), and final decisions regarding their addition were consensual (LK/ES). The ICPC code P02 had a low positive predictive value (PPV) for anxiety problems and was therefore not included in the quantitative analysis (Supplementary table S5: PPV algorithm).
Characteristics of children presenting with anxiety problems and GPs’ management (qualitative analyses)

For each case the following variables were extracted automatically: age at presentation, sex, history of psychosocial problems (any P-code/any Z-code) and healthcare use (any blood-tests, number of consultations with GP) in the two years before presentation, pharmacological management from two years before until two years after presentation (psychiatric medication including antipsychotics, antidepressants, anxiolytics, and hypnotics (ATC N05-N07) and beta-blockers (ATC C07)).

The following information was extracted manually (LK), using quantitative content analysis, by reading medical files from two years before until two years after presentation and by counting the respective occurrence: healthcare use in the two years before presentation (i.e. any referrals to specialist medical care, any visits to emergency care), associated factors described in the GPs’ notes/specialists’ letters in two years before until two years after presentation (i.e. marital status of parents, presence of domestic violence/maltreatment, victim of sexual violence/crime/bullying, fear of failure, sleeping problems, school problems/absenteeism and concentration problems), GPs’ management in the first year after presentation (i.e. any referral, type of referral, number of consultations until referral). Referrals were classified as: 1st referral to primary or specialised mental healthcare, and 2nd referral to paediatrician. Additionally, involvement of YMHPNs within general practice, and the number of consultations with YMHPNs were extracted manually.

Statistics

Incidence rates were determined by dividing the number of cases which received a first ICPC code for anxiety (P01 or P74) by the total number of person-years at-risk and are expressed per 1000 person-years. Incidence rates were analysed by age-group (young children: 0-6 years; children: 7-12 years; adolescents: 13-17 years) and sex (male vs female).(41) Person-years at-risk were defined as actual time-at-risk in years, that children (<18 years, without ICPC coded anxiety) contributed to our database.

Descriptive statistics were used to describe patient characteristics and the GPs’ management. Statistical analysis of differences in proportions between sex and age categories were performed using the Pearson chi-square test and Fisher’s exact test, and Student’s t-test for testing for statistical significance of observed means. Due to the exploratory nature of our study, no adjustments for multiple testing were performed. Analyses were performed using R (version 4.0.0, R Core Team, 2020).

Reporting and ethical considerations:
We adhered to the RECORD guidelines for the reporting of studies using electronic health records.(42) Under Dutch GDPR law, our study does not require ethical approval. RPCD is a pseudonymized, opt-out database. RPCD is stored confidentially on a local server of ErasmusMC. Patients are informed by their GP about the participation of the practice, and that their information can be removed from the database upon their request. Our study was approved by the RPCD steering committee on November 12, 2019 (project number 2019-010).

Results

Study population

In total, 51,212 children aged 0-17 years were included in our cohort between 2012 and 2018. The median age was 8.7 years and 50.8% were male. The number of registered children in our database increased from 21,140 children in 2012 to 35,190 children in 2018. The general characteristics of children remained comparable over time (Supplementary table S1).

Incidence of ICPC coded anxiety (P01/P74) (quantitative analyses)

During the study period, 949 children were coded for the first time with ICPC P01 or P74. Median age at coding was 13.2 years (IQR 9.1-16.3) and 61.6% were female. The overall incidence was 5.36 (95%CI 5.02-5.71) per 1000 persons-years at-risk (PYAR). The incidence was higher for girls than boys with an incidence rate ratio (IRR) of 1.66 (95%CI 1.46-1.89). Girls aged 13-17 years had the highest incidence rate with 14.01 (95%CI 12.55-15.58) per 1000 PYAR (Figure 2; Supplementary table S2/S3 for incidence rate per category and year).

Characteristics of children presenting with anxiety problems (qualitative analysis)

In total, we included 381 children presenting with anxiety problems to their GP (Figure 1). Of these, 154 were male (40.4%) and 227 were female (59.6%). Median age at presentation was 13.3 years. Girls were older at presentation than boys (14.0 years vs 12.2 years respectively, p=0.02).

During the 2-year run-up period, children consulted their GP with a median of five times in two years (Table 1). In this period, 22.6% were coded with a psycho-social problem (any P-code other than P01/P02/P74), and 6.0% received one or more prescriptions of psychiatric medication (ATC N05-N07). Healthcare use in the run-up period was comparable for boys and girls. There was a trend in different healthcare use between age groups (Table 1), with young children being referred more often, and older children undergoing more blood tests.
GPs’ management (qualitative analysis)

During the first year after presentation with an anxiety problem children had a median of one consultation (IQR 1-2) with their GPs concerning the anxiety problem. In total 72.7% of children were referred within the first year either externally to mental healthcare providers or paediatricians, or internally to the YMHPN (Table 3). If additional mental health providers were engaged, in 75.7% of cases the GP decided to involve them at the first consultation. In 59.3% of cases, children were referred to external mental healthcare providers. In cases of referral to paediatricians (5.0%), anxiety problems were accompanied by physical symptoms. 26.5% of cases were seen by a YMHPN, with a median of 3 contacts (IQR 1-4.5). 15.2% of all children (that is 57.4% of the children seen by a YMHPN) were seen by YMHPNs and referred externally to mental healthcare providers in the year after presentation (Table 3). Usually, these children were first seen by a YMHPN and later referred to mental healthcare providers, but the exact order of referral could not always be verified.

Of all children referred to mental healthcare, 40.0% of the medical records contained a specialist letter with conclusive information about diagnosis or treatment. Referring to these children, 31.5% received an anxiety disorder diagnosis by a psychologist or psychiatrist with an anxiety disorder, 28.7% received treatment for anxiety problems without receiving a formal anxiety disorder diagnosis, and 9.3% was diagnosed with post-traumatic stress disorder and 30.5% of children received other diagnoses (either autism, ADHD, or behavioral disorders).

Pharmacological treatment

In the first year after presentation, 10.5% of children received at least one GP prescribed psychiatric medication (ATC N05-N07; see Table 4). The prescription rate was the highest for adolescents aged 13-17 years (14.1%). Benzodiazepines were prescribed to 5.5% of children in the year after presentation, mainly to adolescents, with 9.1% of adolescents receiving at least one prescription. Beta-blockers were only prescribed to adolescents, with 16.7% of adolescents receiving at least one prescription within one year.

Discussion

Summary

The incidence of ICPC codes P01/P74 was 5.36 per 1000 persons-years at-risk (PYAR). Girls were more often affected than boys. The highest incidence rate of 14.01 per 1000 PYAR was in adolescent girls. GPs referred 59.3% of children presenting with an initial anxiety problem to external mental
healthcare providers, YMHPNs were involved in 26.5% of cases. In the year after presentation, 10.5% of children, especially adolescents, received a psychiatric prescription.

**Strengths and weaknesses**

Our study combines the advantages of a large dynamic cohort (using quantitative data from medical files) with in-depth qualitative analyses of selected medical files. For our qualitative analysis, we reviewed children with clinically relevant follow-up period of 4 years or more who presented to their GP with anxiety problems. We were able to create a sensitive search algorithm for children presenting with first anxiety problems to their GP, using both ICPC codes and free-text (Supplementary table S4/S5).

Our study has also limitations. Firstly, for logistical reasons, GPs’ notes are often concise and information on symptoms and associated problems might not always have been documented. Secondly, incorrect or imprecise coding by healthcare professionals is a disadvantage of using electronic health care databases and can cause under- and over-estimation of the frequency of symptoms and diseases. In our qualitative search, we found that children coded with P02 sometimes had relevant anxiety complaints. Therefore, our incidence rate of ICPC coded anxiety (P01/P74) may underestimate the frequency of paediatric anxiety problems. Thirdly, because GPs do usually not give a formal diagnosis of anxiety disorders nor do they use standardized screening/classification tools, it is difficult to differentiate between milder and severe anxiety problems in our database. Fourthly, only GPs’ prescriptions of medications can be extracted from the RPCD, without being clear whether the medication was started by the GP or a specialist. Fifthly, RPCD consists of practices in a restricted (sub)urban area, it remains uncertain whether our results are generalizable to other regions. Finally, not all practices in the RPCD had a YMHPN during the study period. Because of anonymized information, we were not able to differentiate between practices with and without YMHPNs in our analyses.

**Comparison with existing literature**

In a UK primary care registry study and a Danish secondary care registry study the incidence of anxiety disorders varied between 1.8-2.6 cases per 1000 PYAR, (34, 35) considerably smaller incidences as compared with our incidence of ICPC coded anxiety of 5.36. In our study girls had an increased risk of receiving an ICPC code for anxiety compared with boys (IRR: 1.66), which is in line with previous studies.(28, 34, 35) Compared with our findings, a Norwegian study using primary and secondary healthcare data found a higher prescription rate of anxiolytic medication.(43) Further, our finding that GPs frequently involve additional mental health specialists and YMHPNs when
confronted with children with a new anxiety problem confirms conclusions from previous studies that GPs refrain from managing children with psychological problems, (18, 36) and that GPs saw their role mainly as gate-keepers, referring children to specialized healthcare providers.(18)

Differences between our findings and findings from other countries are probably partially to be explained by methodological differences (e.g., differences in inclusion criteria) but may also indicate relevant differences in the occurrence and management of anxiety problems between different countries.

Implications for research and practice

In line with other studies, we found a peak incidence of ICPC coded anxiety in adolescent girls.(28, 34, 35) Therefore, it seems relevant for GPs to consider anxiety problems with children, especially adolescent girls, presenting with possibly related problems, such as headaches, recurrent abdominal pain and sleeping problems.(44-46) The hesitancy of GPs to manage paediatric anxiety problems combined with a comparably high prescription rate of benzodiazepines and beta-blockers raises concerns regarding the adequate management of paediatric anxiety problems in general practice, given both medications are not routinely indicated for children, and that benzodiazepines pose a risk of abuse.(47) In this context, it seems advisable for GPs to refer not only younger children, but also adolescents with anxiety problems to additional screening and counselling by a mental health care professional, rather than prescribing benzodiazepines or beta-blockers.

Since 2015 YMHPNs have been introduced in Dutch general practices in order to support the management of psychological problems within general practice settings.(26, 27) Our study shows that YMHPNs were already involved in the management of more than a quarter of children aged 7-17 years with anxiety problems. Future research should investigate whether the introduction of YMHPNs has improved the availability of treatment opportunities for children with anxiety problems and should evaluate the effectiveness of the shared approach involving GPs and YMHPNs. If proven effective, the introduction of YMHPNs could offer an integrational solution to the observed treatment gaps for paediatric psychological problems, and to the apparent hesitancy of GPs to become involved with psychological problems.

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Figure 1: patient selection for incidence calculation ‘ICPC coded anxiety’ and qualitative analyses of ‘children presenting with anxiety problems’
Figure 2: Incidence rate of ‘ICPC coded anxiety’ per age category
Table 1 Comorbidities and healthcare use in two years before presentation with an anxiety problem

| Comorbidities & healthcare use                                                                 | Overall N=381 | Boys N=154 | Girls N=227 | 0-6 years N=37 | 7-12 years N=146 | 13-17 years N=198 | Boys vs Girls** | Age categories** |
|------------------------------------------------------------------------------------------------|---------------|------------|-------------|----------------|-------------------|-------------------|-----------------|-----------------|
| Total consultations in general practice                                                      | 5 (3-9)       | 5 (3-8)    | 5 (3-9)     | 7 (5-9)        | 4 (2-7)           | 5 (3-9)           | p=0.16          | p=0.002         |
| Previous mental health problem (any ICPC P-code)                                              | 22.6%         | 21.4%      | 23.3%       | 21.6%          | 28.1%             | 18.7%             | p=0.75          | p=0.12          |
| Previous social problem (any ICPC Z-code)                                                     | 9.4%          | 12.3%      | 7.5%        | 18.9%          | 8.2%              | 8.6%              | p=0.16          | p=0.12          |
| ≥1 Prescription of psychiatric medication                                                      | 6.0%          | 5.2%       | 6.6%        | 0.0%           | 3.4%              | 9.1%              | p=0.73          | p=0.03          |
| ≥1 Blood test                                                                                  | 35.4%         | 31.8%      | 37.9%       | 21.6%          | 24.7%             | 46.0%             | p=0.27          | p<0.001         |
| ≥1 Referrals to mental health or hospital specialist                                            | 42.3%         | 46.8%      | 39.2%       | 62.2%          | 47.3%             | 34.8%             | p=0.17          | p=0.003         |
| ≥1 Visit to emergency department in the year before diagnosis*                                 | 24.9%         | 29.9%      | 21.6%       | 48.6%          | 24.0%             | 21.2%             | p=0.09          | p=0.002         |

* In one year before diagnosis.
** Percentages among boys compared with girls, percentages among age categories, compared with the Chi2 test. These hypothesis tests are of exploratory nature, and are therefore not corrected for multiple testing.
Table 2 Associated problems reported in patient journal

| Percentage with* | Overall  | Boys   | Girls  | 0-6 years | 7-12 years | 13-17 years | Boys vs Girls** | Age categories** |
|------------------|---------|--------|--------|-----------|------------|-------------|----------------|-----------------|
|                  | N=381   | N=154  | N=227  | N=37      | N=146      | N=198       |                 |                 |
| Divorced parents or single caregiver | 19.4% | 13.0% | 23.8% | 16.2% | 21.2% | 18.7% | p=0.01 | p=0.73 |
| Domestic violence or child maltreatment | 9.4%  | 8.4%  | 10.1% | 16.2% | 6.2%  | 10.6% | p=0.71 | p=0.15 |
| Victim of sexual violence | 6.3%  | 5.2%  | 7.0%  | 2.7%  | 3.4%  | 9.1%  | p=0.61 | p=0.08 |
| Victim of crime | 10.2%  | 11.7% | 9.3%  | 16.2% | 11.0% | 8.6%  | p=0.55 | p=0.35 |
| Victim of bullying | 15.0% | 16.2% | 14.1% | 10.8% | 17.8% | 13.6% | p=0.67 | p=0.43 |
| Fear of failure | 26.0% | 23.4% | 27.8% | 21.6% | 18.5% | 32.3% | p=0.40 | p=0.01 |
| Sleeping problems | 37.0% | 36.4% | 37.4% | 40.5% | 43.8% | 31.3% | p=0.91 | p=0.05 |
| School problems | 46.2% | 44.2% | 47.6% | 45.9% | 45.9% | 46.5 | p=0.58 | p=0.99 |
| School absenteeism | 20.7% | 22.7% | 19.4% | 5.4%  | 21.2% | 23.3% | p=0.51 | p=0.05 |
| Concentration problems | 20.0% | 19.5% | 20.3% | 10.8% | 18.5% | 22.7% | p=0.95 | p=0.21 |

*Percentage known with characteristic at any point from 2 years before presentation until 2 years after presentation.

**Percentages among boys compared to girls, percentages among age categories, compared with chi2 test. These hypothesis tests are of exploratory nature, and are not corrected for multiple testing.
### Table 3 GPs’ management of anxiety problems in first year after presentation

| Measure                                                                 | Overall N=381 | Boys N=154 | Girls N=227 | 0-6 years N=37 | 7-12 years N=146 | 13-17 years N=198 | Boys vs Girls** | Age categories** |
|------------------------------------------------------------------------|---------------|------------|-------------|----------------|------------------|------------------|-----------------|-----------------|
| Median contacts with GP for anxiety (IQR)                              | 1 (1-2)       | 1 (1-2)    | 1 (1-2)     | 1 (1-2)        | 1 (1-2)          | 1 (1-2)          | p=0.87          | p=0.87          |
| Referral for anxiety either external or by internal involvement of YMHPN (%) | 72.7%         | 67.5%      | 76.2%       | 86.5%          | 78.1%            | 66.2%            | p=0.08          | p=0.007         |
| External referral to mental health care (%)                            | 59.3%         | 58.4%      | 60.0%       | 78.4%          | 71.9%            | 46.5%            | p=0.86          | p<0.001         |
| External referral to paediatrician (%)                                 | 5.0%          | 4.5%       | 5.3%        | 5.4%           | 4.8%             | 5.1%             | p=0.09          | p=0.13          |
| Involvement YMHPN (%)                                                  | 26.5%         | 20.1%      | 30.8%       | 8.1%           | 21.2%            | 33.9%            | p=0.03          | p<0.001         |
| Median contacts with practice nurse (IQR)                              | 3 (1-4.5)     | 2 (1-4.75) | 3 (1-4)     | 2 (1.5-2)      | 2 (1.4-2.5)      | 3 (1-5)          | p=0.52          | p=0.40          |
| Involvement of YMHPN and external referral mental health care (%)*     | 15.2%         | 11.7%      | 17.6%       | 5.4%           | 15.1%            | 17.2%            | p=0.15          | p=0.19          |

*Children seen by YMHPN and externally referred to mental health care in first year after presentation. 57.2% of children seen by YMHPN were also externally referred.

**Percentages among boys compared to girls, percentages among age categories, compared with chi2 test. These hypothesis tests are of exploratory nature, and are not corrected for multiple testing.
Table 4 Psychiatric medication prescriptions

|                                                                 | Overall | Boys | Girls | 0-6 years | 7-12 years | 13-17 years | Boys vs Girls** | Age categories** |
|------------------------------------------------------------------|---------|------|-------|-----------|------------|--------------|----------------|----------------|
| Psychiatric prescription: 1st year after diagnosis              | 10.5%   | 8.4% | 11.9% | 2.7%      | 7.5%       | 14.1%        | p=0.36          | p=0.03          |
| Psychiatric prescription: 2nd year after diagnosis              | 8.4%    | 7.1% | 9.3%  | 2.7%      | 4.1%       | 12.6%        | p=0.59          | p=0.01          |
| Psychiatric prescription: 0-2 years after diagnosis             | 13.6%   | 9.7% | 16.3% | 5.4%      | 8.2%       | 19.2%        | p=0.09          | p=0.004         |
| SSRI prescription: 1st year after diagnosis                     | 1.0%    | 0.0% | 1.8%  | 0.0%      | 0.0%       | 2.0%         | p=0.15          | p=0.15          |
| SSRI prescription: 2nd year after diagnosis                     | 1.6%    | 0.6% | 2.2%  | 0.0%      | 0.0%       | 3.0%         | p=0.43          | p=0.06          |
| SSRI prescription: 0-2 years after diagnosis                    | 1.8%    | 0.6% | 2.6%  | 0.0%      | 0.0%       | 3.5%         | p=0.26          | p=0.05          |
| Benzodiazepine prescription: 1st year after diagnosis           | 5.5%    | 3.9% | 6.6%  | 0.0%      | 2.1%       | 9.1%         | p=0.36          | p=0.006         |
| Benzodiazepine prescription: 2nd year after diagnosis           | 2.1%    | 2.6% | 1.8%  | 0.0%      | 0.0%       | 4.0%         | p=0.72          | p=0.03          |
| Benzodiazepine prescription: 0-2 years after diagnosis          | 6.0%    | 5.2% | 6.6%  | 0.0%      | 2.1%       | 10.1%        | p=0.73          | p=0.004         |
| Beta-blocker prescription: 1st year after diagnosis             | 8.7%    | 6.5% | 10.1% | 0.0%      | 0.0%       | 16.7%        | p=0.29          | p<0.001         |
| Beta-blocker prescription: 2nd year after diagnosis             | 2.1%    | 2.0% | 2.2%  | 0.0%      | 0.0%       | 4.0%         | p=1.00          | p=0.04          |
| Beta-blocker prescription: 0-2 years after diagnosis            | 9.2%    | 6.5% | 11.0% | 0.0%      | 0.0%       | 17.7%        | p=0.19          | p<0.001         |

* ≥1 psychiatric prescriptions of ATC classification N05-N07.
**percentages among boys compared to girls, percentages among age categories, compared with chi2 test. These hypothesis tests are of exploratory nature, and are not corrected for multiple testing.**