

The Use of Antidepressants, Antipsychotics, and Stimulants in Youth Residential Care

Beate Oerbeck, PhD,¹ Kristin Romvig Overgaard, MD, PhD,¹ Vidar Hjellvik, PhD,²
Lars Lien, MD, PhD,^{3,4} and Jørgen G Bramness MD, PhD^{3,5,6}

Abstract

Objectives: To assess the use of three commonly prescribed psychotropic medications in youth placed in residential care (RC).

Methods: Participants were youth aged 0–20 years placed in RC institutions at least once during 2016. Data on filled prescriptions were taken from the Norwegian Prescription Database to compare the use of antidepressants, antipsychotics, and stimulants in RC with the age- and gender-adjusted general child population (GenPop) and how this co-varied with reasons for RC placement, age, and gender.

Results: One thousand eight hundred fifty-six children and adolescents were identified in RC, with mean age 14 (range 0–20 years), 46% girls, 81% ≥ 13 years. Among those, 423 or 23% used any of the 3 psychotropics, which was significantly more than the 3.7% in GenPop. The prevalence ratios RC/GenPop were 6.6 for antidepressants, 17.9 for antipsychotics, and 4.4 for stimulants. The median number of days per year for the dispensed defined daily doses varied from 8.3 to 244.0 for the different antipsychotics, indicating short time use for most of the people. Polypharmacy was not frequent in RC, as only 26% used ≥ 2 classes of medication, but still significantly more frequent than the 10% in GenPop. Youth placed in RC for serious behavior problems had significantly higher use of stimulants than those with other placement reasons. Psychotropics were not used below age 6 years, and although the use of antidepressants and antipsychotics overall increased with age, stimulants were mostly used by 6–16-year olds. The girl/boy ratio for any psychotropic medication use in RC was 1.4 (95% confidence interval [95% CI]: 1.1–1.6), significantly higher than the corresponding ratio in GenPop: 1.0 (95% CI: 0.9–1.0).

Conclusion: The present findings do not necessarily suggest an overtreatment with medication in RC. However, the frequent short-term use of antipsychotics, presumably for non-psychotic symptoms, is a concern, as it may reflect that the youth are not provided with the recommended first-line psychological treatments.

Keywords: child welfare, psychotropic medication, antidepressants, antipsychotics, stimulants

Introduction

STUDIES OF YOUTH within different sectors of the U.S. child welfare system have reported high rates of psychiatric and/or neurodevelopmental disorders (Garland et al. 2001; Turney and Wildeman 2016). Similar high rates were confirmed in a large British study, with a significantly higher prevalence among those in residential care (RC) (71%) compared with foster care (39%) (Ford et al. 2007). In a recent representative study using a structured psychiatric interview, 76% of Norwegian adolescents in RC were reported to have at least one psychiatric disorder (Jozefiak et al.

2016). Anxiety- and depressive disorders were more prevalent than behavioral disorders, with a high comorbidity between the two main types of disorders. The high number of psychiatric disorders is not surprising, given the reasons for placement in RC, that is, severe psychosocial strain, neglect, maltreatment, and/or serious behavioral problems, all represent risk factors for mental disorders (Gilbert et al. 2009; Green et al. 2010; Hunt et al. 2017). Of note, although a great majority of the adolescents in RC were diagnosed with a psychiatric disorder, only 38% had received help from the child and adolescent mental health services (Jozefiak et al. 2016).

¹Division of Mental Health and Addiction, Oslo University Hospital, Oslo, Norway.

²Department of Chronic Diseases and Ageing, Norwegian Institute of Public Health, Oslo, Norway.

³Norwegian National Advisory Unit on Concurrent Substance Abuse and Mental Health Disorders, Innlandet Hospital Trust, Hamar, Norway.

⁴Faculty of Health and Social Science, Inland University College of Applied Science, Elverum, Norway.

⁵Department of Alcohol, Tobacco and Drugs, Norwegian Institute of Public Health, Oslo, Norway.

⁶Institute of Clinical Medicine, UiT—The Arctic University of Norway, Tromsø, Norway.

Funding: The present study had no specific funding and was carried out as part of the authors' clinical positions.

As many major psychiatric disorders have an onset before age 18, medication has been increasingly utilized in youth, but, as pointed out in an important review about 10 years ago, psychopharmacologic treatments in pediatric patients also raised concerns regarding a potential overtreatment, without adequate data regarding the pediatric efficacy and safety of psychotropic classes (Correll et al. 2011). The authors still concluded that for three frequently used classes, that is, stimulants, antidepressants, and antipsychotics: “effect sizes against placebo have typically been at least moderate, with most numbers-needed-to-treat well below 10 for response, indicating clinical significance as well.”

In a more recent review, stimulants, selective serotonin reuptake inhibitors (SSRIs), and antipsychotics were found to have documented efficacy for attention-deficit/hyperactivity disorder (ADHD), pediatric depression/anxiety disorders, and childhood-onset schizophrenia, respectively (Giles and Martini 2016). The review also reported that the evidence base for providing antipsychotics to youth with bipolar mania and autism spectrum disorders (ASD) had grown, and that atypical antipsychotics were used in the pediatric population for the management of aggressive and oppositional behaviors, although there were concerns regarding adverse reactions. Further, a study of dosage and prevalence of antipsychotic prescriptions in Scandinavia from 2006 to 2016 found a steady trend of low or decreasing dosages for the majority of commonly used antipsychotics, suggesting that these are prescribed outside their main indications (e.g., as anxiolytics, hypnotics or sedatives) (Hojlund et al. 2019).

The use of psychotropic medication has been found to vary considerably between countries, as also confirmed in the recent international review, where U.S. youth consistently were found among the high users (Piovani et al. 2019). The review reported that the global random-effect pooled prevalence of psychotropic drug prescriptions among youth was 15.3‰ (95% confidence interval [CI] 7.6‰–25.7‰) for ADHD medications, 6.4‰ (95% CI 4.3–8.7) for antidepressants, and 5.5‰ (95% CI 3.6–7.8) for antipsychotics. Systematic monitoring was found to be lacking in most countries, and the authors noted that prevalence data by gender were often missing.

In a study of U.S. national annual prescribing patterns of the same three psychotropic classes, data from different age groups were analyzed from a national longitudinal prescription database ($n=6,351,482$) (Sultan et al. 2018). The total annual percentage of prescriptions filled by youth for any of the three classes was by age 3–5 years: 0.8%, 6–12 years: 5.4%, 13–18 years: 7.7%, and 19–24 years: 6.0%. Stimulant use was highest for older children (age 11=5.7%). Antidepressant use tended to increase with age and was highest for young adults (age 24=4.8%). Annual antipsychotic prescription percentages were lower than antidepressant or stimulant percentages for all age groups, with a peak in adolescence (age 16=1.3%). Annual stimulant and antipsychotic percentages for males were higher than corresponding percentages for females, but they converged for young adults.

Within the child welfare system, there is still a paucity of studies on psychotropic medication use, and systematic data on patterns of medication treatment, with a particular weight on the use of concomitant drugs has been called for in the literature (Raghavan et al. 2005; Zito et al. 2008b). In the following, we therefore include relevant literature from the last two decades.

An early report on Medicaid-enrolled youth in foster-care raised concern as 30% had received psychotropic medications (dosReis et al. 2001). Following up with a later study, the most frequently used medications were antidepressants (57%), ADHD drugs (56%), and antipsychotics (53%) (Zito et al. 2008b) with frequent poly-

pharmacy, as 41% of the youth in foster care received ≥ 3 different classes of psychotropics, and the authors were concerned, as polypharmacy increases the risk for adverse reactions (Bogler et al. 2019). Later studies have corroborated the high prevalence of polypharmacy and demonstrated subgroup differences, such as higher polypharmacy in boys compared with girls, and in group homes compared with foster homes (Keast et al. 2019).

Although it is difficult to accurately compare the prevalence of psychotropic medications due to different jurisdictions and different years and age groups reported in the literature, the prevalence rates for the use of at least one psychotropic agent in U.S. child welfare has been found to be as high as 37% in older youth in foster care (McMillen et al. 2004), and even used by the majority of the study participants in therapeutic foster care (67%) and group homes (77%) (Breland-Noble et al. 2004).

A recent review on psychotropic medications for different groups of highly vulnerable children in the United States concluded that they generally receive numerous psychotropic medications. This includes high rates of polypharmacy, off-label use, and long-term use, typically in the absence of adjunctive psychosocial interventions (McLaren et al. 2018). The authors further reported medication use among 76%–91% of the children within residential treatment facilities, compared with 7.5% in the general child population, and 13%–40% in children placed in foster care.

In a literature search on psychotropic medication use in child welfare, the retrieved studies were generally from the United States, as presented earlier, and none were from developing countries. We found only one Scandinavian study, showing that about one-third of youth institutionalized for serious behavioral problems in two Swedish adolescent units were given psychopharmacological treatment (Anckarsäter et al. 2007). This lack of studies is unfortunate as Scandinavian countries have prescription databases available for all citizens, providing opportunities to inform on representative populations.

To the best of our knowledge, representative Scandinavian studies of the use of antidepressants, antipsychotics, and stimulants have not been investigated in the child welfare system. The aim of the present study was, therefore, to investigate the use of these three commonly used classes of psychotropic medication in a representative Norwegian cohort of youth placed in RC institutions, including how this varied with reasons for placement, age, and gender.

Methods

Study population

Participants were all children and adolescents aged 0–20 years placed in RC institutions under the Norwegian Directorate for Children, Youth and Family Affairs, Child Welfare Services (BUFDIR) at least once during 2016 due to one or more of the following reasons for placement: neglect, emergency placement, serious behavioral problems of high and low degree, and/or substance abuse. This directorate is responsible for all RC institutions in Norway except for those in the municipality of Oslo, which administers its own institutions. Consequently, 80% of Norwegian RC institutions were included in the present study. Available background data on the participants included gender, age, and reasons for placement in RC institutions.

Prescription drug data

For the RC population, data on all filled prescriptions during 2016 were available from the Norwegian Prescription Database (NorPD) for each individual. The drugs were classified according to

the Anatomical Therapeutic Chemical (ATC) classification system, version 2020 (World Health Organization [WHO] 2020) available from https://www.whocc.no/atc_ddd_index_and_guidelines/guidelines.

We had information on ATC code and month of dispensing. For the general population we had information on number of users of the relevant ATC codes in 2016 in 1-year age groups for boys and girls. The following classes of psychotropic medications were studied: antidepressants (ATC N06A), antipsychotics (ATC N05A, except N05AN01 [lithium]), and stimulants (ATC N06BA), defined as at least one prescription of one of the relevant psychotropic medication classes during 2016. In Norway, the number of children and adolescents treated with lithium or other mood stabilizers were low (Bramness et al. 2009; Furu et al. 2018), and we were therefore unable to report these frequencies in our population. The quantity dispensed for each drug prescription is expressed by the defined daily dose (DDD) measure, which is “the assumed average maintenance dose per day for a drug used for its main indication in adults” (WHO 2020).

Statistics

We compared the prevalence of dispensed psychotropic medication in RC with the age- and gender-corrected prevalence in the general child population (GenPop). We also compared boys and girls within and between the two populations. Means, percentages, and prevalence ratios (PRs) with 95% CIs are presented. $PR = (n_{RC}/N_{RC}) / (n_{GenPop}/N_{GenPop})$, where n and N denote number of users and number of individuals, respectively, in the two populations. Age- and gender correction was done by using the “ageadjust.direct” function in the R-package epitools, with the study population as reference population (1 year age groups). PRs between girls and boys and between RC and GenPop, with 95% CIs were computed by using the “riskscoreci” function in the “PropCIs” package in R (R Development Core Team 2020). p -Values for PRs in the study population were computed by using Fisher’s exact test. When the numerator and/or the denominator of the PR was age- and gender corrected, the uncertainty involved in the age- and gender correction was taken into account by using a simulation approach (see Supplementary Data for details). We calculated the median, lower, and upper interquartile of DDDs per person per year, thereby estimating the median number of days for which each person was treated with the different psychotropic medications during 2016.

The chi-square test was used to compare polypharmacy in RC with GenPop, and medication use with reasons for placement in RC.

Ethics

The study was approved by The Regional Committee for Medical Research Ethics in South-Eastern Norway (REK), Norwegian Centre for Research Data, and the Norwegian Data Inspectorate without informed consent under given conditions. These conditions included data only being handled by one of the authors (V.H.) on a secure server and destroying the linking key to ensure no possibility for back identification of individuals. Further, data were available in 1-year age groups, but are presented in larger intervals (0–5, 6–12 years, etc.) to ensure anonymity, and numbers less than $N=5$ are not shown. A personal identification number provided by BUFDIR allowed a linkage via the Norwegian National Register to the NorPD prescription data (reference: REK 2017/1637).

Results

One thousand eight hundred fifty-six youth were identified in RC with mean age 14 years (range 0–20 years), 46% girls, 81% ≥ 13 years. Among those, 423 children (23% [95% CI: 20.9–24.8]) dispensed at least one of three psychotropic medications (antidepressants, antipsychotics, or stimulants), which was significantly more than the 3.7% in the general child population (PR: 6.1 [95% CI: 5.6–6.8]).

In RC, polypharmacy was not frequent, as 74% ($n=312$) used one class of medication, 24% ($n=102$) used two, and 2% ($n=9$) used three classes, although significantly more frequent than in GenPop, where 90% ($n=27,791$), 9.5% (2929), and 0.5% (153) of the psychotropic drug users used one, two, and three classes, respectively ($p<0.0001$). Figure 1 displays the use of the three psychotropics and their overlap in boys and girls in RC. Although the combination of antidepressants and antipsychotics was most common among girls, the combination of antipsychotics and stimulants was most common among boys.

In RC, antidepressants were used by 8.9%, antipsychotics by 10.9%, and stimulants by 9.6%. In GenPop the corresponding numbers were significantly lower: 0.7%, 0.4%, and 1.5%, respectively, with PRs between RC and GenPop: 6.6 (95% CI: 5.5–7.8) for antidepressants, 17.9 (95% CI: 15.1–21.2) for antipsychotics, and 4.4 (95% CI: 3.7–5.2) for stimulants.

When comparing reasons for placement in RC (e.g., neglect, emergency placement, serious behavioral problems of high and low degree, and/or substance abuse), overall medication use was significantly different ($p=0.02$), mainly due to higher use of stimulants ($p<0.0001$) among those placed for serious behavior problems. The percentage using stimulants was highest in those placed for serious behavioral problems of a high degree (22.3; 95% CI 15.1–31.8) and lowest in those placed for substance abuse (5.2; 2.2–11.6). For antipsychotics it was the other way round—the percentage was highest in those placed for substance abuse (18.8; 12.2–27.2) and second lowest in those placed for serious behavioral problems of high degree (10.6; 5.9–18.5). The lowest antipsychotic use was in those with emergency placement (10.4; 8.4–13.0). The pattern for antidepressants was similar to that of antipsychotics. Both for antidepressants and antipsychotics, the CIs for all five placement groups overlapped, whereas for stimulants both the high and low degree of serious behavioral problems groups had significantly higher use than the emergency placement, neglect, and substance abuse groups.

None of the children aged 0–5 years in RC used any of the investigated psychotropic medications. The use of any of the 3 psychotropics increased with age and was 13.9% among 6–12-year olds, 23.2% among 13–16-year olds, and 31.1% among 17–20-year olds, which was about 6 times higher than GenPop in all age groups. The girl/boy ratio for any psychotropic medication use in RC was 1.4 (95% CI: 1.1–1.6), significantly higher than the corresponding ratio in GenPop: 1.0 (95% CI: 0.9–1.0).

In RC, antidepressants were not used under age 13 years, but increased with age thereafter (7.6% and 14.5% in the two older age groups). The use of antipsychotics in RC increased with age group (5.7%, 9%, and 16.8%, respectively), and the ratio RC/GenPop was particularly high (33.0) among 6–12-year olds and about 18 in the 2 older age groups. In RC, 13.1% used stimulants among 6–12 olds (ratio RC/GenPop: 5.9) with a 12.7% and 8.9% use in the 2 oldest age groups (and ratios RC/GenPop of about 4).

Gender differences were found between the three classes, with significantly more antidepressants and antipsychotics in girls

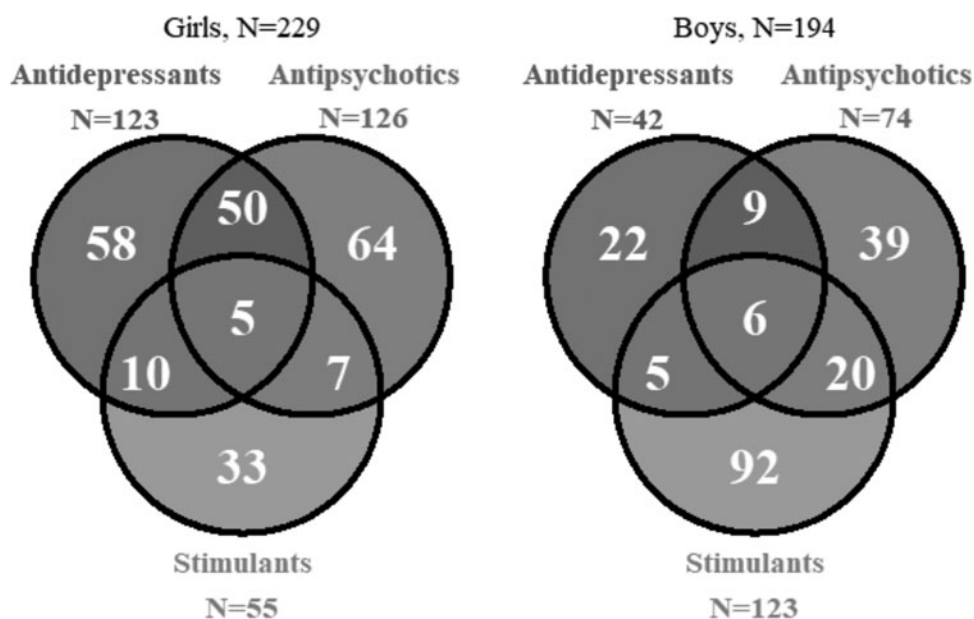


FIG. 1. The use of different psychotropics and their overlap in boys and girls in residential care. Numbers below 5 are shown as 5 to avoid identification of the few youths with combinations of drugs. Some numbers above 5 are adjusted correspondingly to make the total *N* per drug class correct. No number above 5 deviates with more than ±2 from the true number.

compared with boys, and the reverse pattern found for stimulants (girl/boy ratios of 3.4, 2.0, and 0.5, respectively, all *p*'s < 0.001). Please see Supplementary Tables S1–S3 for details on the use of antidepressants, antipsychotics, and stimulants in RC, including ratios RC/GenPop for each age group for all participants, and by gender, as well as girl/boy ratios by age group for the different psychotropics.

Among the 423 in RC who were dispensed psychotropic medication, 39.0% used antidepressants, 47.3% antipsychotics, and 42.1% stimulants. Among antidepressants, SSRIs were used by 83.0%, and the rest used other antidepressants than SSRIs (ATC-code N06A). Among stimulants, methylphenidate was used by 73.6% in RC (the rest used lisdexamfetamine or atomoxetine).

Details of the different antipsychotics used in RC in boys and girls are presented in Table 1, including data for the different age groups when possible (*N* > 5). The median number of days per year

with dispensed DDDs was highest for olanzapine and aripiprazole, and lowest for quetiapine, risperidone, and clorprotixene, indicating that at least these three latter antipsychotics were dispensed sporadically. For all antipsychotics, very few of the children (*N* = 11) in RC were dispensed DDDs, indicating use all year. There were similar median DDDs with overlapping interquartile ranges between age groups, and between girls and boys.

Discussion

The present study compared the use of antidepressants, antipsychotics, and stimulants among youth placed in RC institutions with the age- and gender-corrected general population (GenPop). Nearly 1 in 4 youth in RC (23%) used at least 1 of these psychotropics, which was significantly more than the GenPop (3.7%). This high and disproportionate use in RC is in line with findings from

TABLE 1. DISPENSED ANTIPSYCHOTICS FOR BOYS AND GIRLS IN RESIDENTIAL CARE AT LEAST ONCE IN 2016, INCLUDING MEDIAN NUMBER OF DAYS PER YEAR WITH DISPENSED DEFINED DAILY DOSES AND INTERQUARTILE RANGE

| | Age | DDD (mg) | N | | Median DDD (IQR) | |
|-------------------------|-------|----------|------|-------|------------------|-------------|
| | | | Boys | Girls | Boys | Girls |
| Clorprotixene (Truxal) | 0–20 | 300 | 6 | 23 | 9 (6–14) | 8 (5–12) |
| Aripiprazole (Abilify) | 0–20 | 15 | 13 | 19 | 149 (56–168) | 65 (37–205) |
| | 13–16 | | | | 93 (56–196) | 75 (19–261) |
| | 17–20 | | | | 168 (126–168) | 61 (42–182) |
| Risperidone (Risperdal) | 0–20 | 5 | 29 | 21 | 44 (26–78) | 13 (4–38) |
| | 6–12 | | | | 19 (8–32) | |
| | 13–16 | | | | 61 (44–118) | 10 (5–18) |
| | 17–20 | | | | 50 (20–88) | 21 (6–68) |
| Quetiapine (Seroquel) | 0–20 | 400 | 31 | 84 | 25 (12–38) | 29 (6–76) |
| | 13–16 | | | | 25 (19–31) | 31 (6–80) |
| | 17–20 | | | | 22 (12–38) | 29 (6–69) |
| Olanzapine (Zyprexa) | 0–20 | 10 | 7 | 23 | 224 (98–315) | 98 (56–175) |

For age groups with *N* > 5, median DDD (IQR) is also reported. DDD, defined daily dose; IQR, interquartile range.

previous medication studies in the child welfare system (Raghavan et al. 2005; Zito et al. 2008b; McLaren et al. 2018) and could result from the increased number of mental disorders reported in this vulnerable population (Garland et al. 2001; Ford et al. 2007; Jozefiak et al. 2016; Turney and Wildeman 2016).

Among the youth in RC who used antidepressants, 83% dispensed SSRIs, the same proportion as recently reported among Danish youth on antidepressants (81.8% on SSRIs) (Bachmann et al. 2016), and in line with a population-based multi-national comparison analysis of antidepressants (in year 2000), where SSRIs predominated in the United States, Denmark, and the Netherlands (Zito et al. 2006). The high proportion on SSRIs among antidepressant users is encouraging, as a recent meta-analysis reported this to be more beneficial than placebo in treating anxiety and depressive disorders in children and adolescents (Locher et al. 2017). However, the author underlined that the benefit was small and disorder specific, with a larger drug-placebo difference for anxiety disorders than for other conditions. Response to placebo was large, especially in depressive disorders, and severe adverse events were significantly more common with SSRIs than placebo.

Among those who used psychotropics in RC ($n=423$), 47% used antipsychotics, somewhat fewer than among U.S. youth in foster care, where 53% (Zito et al. 2008b) and 65% (Linares et al. 2013) of those medicated were on antipsychotics. In our study, the median number of days on DDDs generally indicated sporadic or short time use of the antipsychotics, most likely indicating that these were prescribed outside their main indications. They may have been prescribed to treat aggression, in line with reports of antipsychotics being frequently used for this purpose (Daviss et al. 2016), and/or to reduce anxiety, sedation or to induce sleep (Gjerden et al. 2017). This frequent use of antipsychotics in RC, outside their main indications, is a concern, as it may suggest that this population is not provided with the recommended first-line psychological treatments for aggressive behaviors (Connor et al. 2006), anxiety (Zhou et al. 2019) and sleep disorders (Bruni et al. 2018). The median number of days was particularly low for clorprotixene, risperidone, and quetiapine (both boys and girls dispensed DDDs <44 days). Olanzapine and aripiprazole were dispensed for longer periods (median number of days boys: 224, 149 days; girls: 98, 65 days, respectively), but overall somewhat shorter than the 180 and 240 median days reported for Medicaid insured youth and youth in foster care, respectively (Burcu et al. 2014). It is possible that youth dispensing antipsychotics for longer periods were treated for their main indications: schizophrenia, bipolar disorders, or aggression associated with ASD, but as these are rare conditions, it is unlikely that they explain all of this use. Indeed, a national Norwegian study on the use of antipsychotic drugs in 2010 found that children and adolescents who used antipsychotic drugs were predominantly diagnosed with nonpsychotic mental disorders, such as neurodevelopmental disorders among boys and anxiety- or depression disorders among girls (Nesvag et al. 2016), all of which were found to be highly prevalent in the national Norwegian study of adolescents in RC (Jozefiak et al. 2016).

Among stimulants used in RC, 73% of the youth dispensed methylphenidate (20% atomoxetine, 16% lisdexamfetamine), lower than in two European population-based studies, where >90% and 98%, respectively, of youth with ADHD used methylphenidate (Garbe et al. 2012; Oerbeck et al. 2020). Still, that which most used methylphenidate in RC suggests that the clinicians follow the European National Institute for Health and Care Excellence (NICE) guidelines (NG87) that only recommend atomoxetine when psy-

chostimulants are not tolerated or to non-responders (National Institute for Health and Care Excellence 2018).

In the present study, 74% of the youth in RC used only one class of psychotropic medications and 26% used ≥ 2 classes. The combination of antidepressants and antipsychotics was most common in girls and stimulants and antipsychotics among boys, somewhat different from previous studies where polypharmacy was more likely in males (Safer et al. 2003; dosReis et al. 2005; Keast et al. 2019). Although polypharmacy in RC was significantly more frequent than in the GenPop (90% on one class of psychotropic medication), the numbers were considerably lower than rates reported in a U.S. study of children in foster care, where 72% were prescribed two or more psychotropic medications (41% ≥ 3) (Zito et al. 2008b). This U.S.–European discrepancy is also in line with international findings reported from the general child population, where concomitant psychotropic use in the United States was three times as frequent as in Germany and twice as frequent as that in the Netherlands (Zito et al. 2008a), most likely a consequence of the large variability across countries in prescribing medication for child and adolescent psychiatric disorders (Vitiello 2008).

When comparing reasons for placement in RC, no apparent explanations for medication use were found, apart from the higher use of stimulants among those referred for serious behavior problems, in line with the effect that stimulants have on disruptive disorders, whether on ADHD alone or with the often comorbid oppositional defiant and conduct disorders (Connor et al. 2002; Pringsheim et al. 2015). Also, stimulant use was least frequent for those placed in RC for reasons of substance abuse, a positive finding in line with the NICE guidelines (National Institute for Health and Care Excellence 2018).

In the present study, none of the psychotropics were used during preschool years (age group 0–5 years) in either population, but from age 6 years onward, the overall use of psychotropics increased with age. Our finding contrasted with two U.S. studies, where 1.2% of children 4 years or younger received at least 1 psychotropic drug, according to Medicaid data (Garfield et al. 2015), and ~12% of children age 6 and younger in foster care for 365 days or more received at least 1 psychotropic medication over the 3-year study period (dosReis et al. 2014). These prescription rates worried the authors due to the limited evidence supporting safety or efficacy in this age group. As there was no reported use of psychotropics among the preschoolers in our study, we have no such concerns for this particular population. However, the complete lack of use could also suggest that a few preschoolers are provided with sufficient psychiatric health services. Of note was that antidepressants were not used in RC ≤ 12 years, but the high use of antidepressants from age 13 years and onward, and the high use of stimulants in the two medium age groups (6–16 years) is in line with previous findings (Olfson et al. 2002; Piovani et al. 2019).

We found that girls in RC overall used significantly more psychotropic medication than boys, contradicting earlier findings in the literature where boys constitute the majority (Zima et al. 1999; Raghavan et al. 2005; Zito et al. 2008b). However, in line with known epidemiological patterns for antidepressants and stimulants (Linares et al. 2013; Steinhausen and Bisgaard 2014; Sultan et al. 2018; Piovani et al. 2019; Barczyk et al. 2020; Zito et al. 2020), we found that girls in RC used more medication indicated for anxiety and depression, whereas boys used more stimulants, for which ADHD is the main indication. We also found that girls in RC used more antipsychotics than boys, in contrast to the general finding of higher use in boys, both in the general child population (Steinhausen and Bisgaard 2014; Piovani et al. 2019) and within child welfare (Linares et al. 2013; Vanderwerker et al. 2014). One could speculate as to

whether this unexpected gender difference reflects the distribution of the psychiatric disorders (particularly anxiety and depression in girls and neurodevelopmental disorders in boys) for which treatment with antipsychotics increasingly is considered to be an option in the general child population (Nesvag et al. 2016; Hojlund et al. 2019) and within child welfare services (Linares et al. 2013).

In our study, we found a shift in the use of antipsychotics from male preponderance in childhood (< age 13) to female preponderance in adolescence (age >13 years), in line with national prescription data from 2008 to 2017 (Furu et al. 2018) (see Supplementary Table S2 for details).

This shift is in line with the known epidemiological patterns for stimulants and antidepressants, where stimulants are most frequently used in boys during middle childhood and antidepressants in adolescent girls, as was the case in our study, and for instance shown in the New Zealand study with national prescription data from 2016 (Barczyk et al. 2020). In our study, the boys in RC used stimulants twice as frequently as girls, and boys had high overlap in the use of stimulants and antipsychotics (Fig. 1). The girls in RC used antidepressants three times more frequently than boys, with high overlap between antidepressants and antipsychotics among the girls (Fig. 1), and as a great majority in our study were adolescents (81%), this probably explains the higher use of these two psychotropics.

Unfortunately, we did not have diagnostic information in our study and were unable to check whether these assumptions explain the gender differences in antipsychotic use. However, both the National Patient Registry data from all Norwegian Child and Adolescent Mental Health Services (Krogh et al. 2016) (from the same year as our study) and a national study on adolescents in RC (Jozefiak et al. 2016) underline that there is a majority of girls diagnosed with anxiety and depressive disorders during adolescence, in contrast to boys diagnosed with ADHD in middle childhood.

Future studies of children in RC should combine information about psychotropic medications and the psychiatric diagnoses and include gender-specific findings.

Strengths and limitations

A strength of the present study is the use of a national prescription registry, which includes all patients treated with psychotropic medication in Norway, providing valuable information about the dispensed medication in this cohort of youth in RC and as such may be considered representative of clinical practice. Our study has limitations. First, we have valid data on dispensed medication, and thus, primary nonadherence is not an issue, but we have no knowledge of whether the child actually took the medication. Second, the NorPD only provides data for filled prescriptions. Thus, since diagnostic information was not available, we cannot report on the prevalence of psychiatric disorders. Third, regarding co-medication, data on the different dispensed medications indicate that they are used during 2016, not necessarily at the exact same time during that year. However, this pertains to both populations and the comparison with the general population is fair. Fourth, all of the children were not in RC all of 2016, and some medications were dispensed when the children were outside RC. Fifth, we do not have the prescribed dosages for the youth in our study. However, for all antipsychotics the DDDs/per person/year were lower, and for some considerably lower, than the assumed average maintenance dose per day for a drug used long-term for schizophrenia/bipolar disorder in adults, in line with what was reported by clinicians in a survey of antipsychotic medication (Rettew et al. 2015). Finally, we do not know whether the partic-

ipants were adequately assessed for the presence of psychiatric disorders or offered recommended psychological interventions before medication was prescribed.

Conclusions

In this representative population of youth in RC, approximately one in four used antidepressants, antipsychotics, and/or stimulants, suggesting a high prevalence of psychiatric disorders in RC. However, given the high prevalence of psychiatric disorders previously reported in this population, the present findings do not necessarily suggest an overtreatment with psychotropic medication in RC. However, the frequent use of antipsychotics is a concern, as it may reflect that the youth are not provided with the recommended first-line psychological treatments for aggressive behaviors, anxiety/depression, or sleep disorders. This concern is supported by previous literature underlining that children within the child welfare system generally do not receive adequately assessment and nonpharmacological treatment. Altogether, the findings in the present study support the need for additional studies that specifically target medication use in conjunction with evidence-based psychological treatments to improve the diagnoses and treatments of mental disorders in this population.

Clinical Significance

Clinicians should ensure that youth in RC are adequately assessed, monitored, and also provided with suitable nonpharmacological treatment when treating them with psychotropic medication, particularly with antipsychotics.

Acknowledgements

We thank librarian Ellen Bjoernstad, Oslo University Hospital, for the literary searches.

Disclosures

No competing financial interests exist.

Supplementary Material

Supplementary Data
Supplementary Table S1
Supplementary Table S2
Supplementary Table S3

References

- Anckarsäter H, Nilsson T, Ståhlberg O, Gustafson M, Saury J-M, Råstam M, Gillberg C: Prevalences and configurations of mental disorders among institutionalized adolescents. *Dev Neurorehabil* 10:57–65, 2007.
- Bachmann CJ, Aagaard L, Burcu M, Gleaske G, Kalverdijk LJ, Peterson I, Schuling-Veninga CCM, Wjllars L, Zito JM, Hoffmann F: Trends and patterns of antidepressant use in children and adolescents from five western countries, 2005–2012. *Eur Neuropsychopharmacol* 26:411–419, 2016.
- Barczyk ZA, Rucklidge JJ, Eggleston M, Mulder RT: Psychotropic medication prescription rates and trends for New Zealand children and adolescents 2008–2016. *J Child Adolesc Psychopharmacol* 30: 87–96, 2020.
- Bogler O, Roth D, Feinstein J, Strzelecki M, Seto W, Cohen E: Choosing medications wisely: Is it time to address paediatric polypharmacy? *Paediatr Child Health* 24:303–305, 2019.

- Bramness JG, Groholt B, Engeland A, Furu K: The use of lithium, valproate or lamotrigine for psychiatric conditions in children and adolescents in Norway 2004–2007—A prescription database study. *J Affect Disord* 117:208–211, 2009.
- Breland-Noble AM, Elbogen EB, Farmer EM, Dubs MS, Wagner HR, Burns BJ: Use of psychotropic medications by youth in therapeutic foster care and group homes. *Psychiatr Serv* 55:706–708, 2004.
- Bruni O, Angriman M, Calisti F, Comandini A, Esposito G, Cortese S, Ferri R: Practitioner review: Treatment of chronic insomnia in children and adolescents with neurodevelopmental disabilities. *J Child Psychol Psychiatry* 59:489–508, 2018.
- Burcu M, Zito JM, Ibe A, Safer DJ: Atypical antipsychotic use among Medicaid-insured children and adolescents: Duration, safety, and monitoring implications. *J Child Adolesc Psychopharmacol* 24: 112–119, 2014.
- Connor DF, Carlson DA, Chang KD, Daniolos PT, Ferziger R, Findling RL, Huchinson JG, Malone RP, Halperin JM, Plattner B, Post RM, Reynolds DL, Rogers KM, Saxena K, Steiner H; Stanford/Howard/AACAP Workgroup on Juvenile Impulsivity and Aggression: Juvenile maladaptive aggression: A review of prevention, treatment, and service configuration and a proposed research agenda. *J Clin Psychiatry* 67:808–820, 2006.
- Connor DF, Glatt SJ, Lopez ID, Jackson D, Melloni RH: Psychopharmacology and aggression-1: A meta-analysis of stimulant effects on overt/covert aggression-related behaviors in ADHD. *Database of Abstracts of Reviews of Effects (DARE): Quality-Assessed Reviews*. York, UK, Centre for Reviews and Dissemination, 2002.
- Correll CU, Kratochvil CJ, March JS: Developments in pediatric psychopharmacology: Focus on stimulants, antidepressants, and antipsychotics. *J Clin Psychiatry* 72:655–670, 2011.
- Daviss WB, Barnett E, Neubacher K, Drake RE: Use of antipsychotic medications for nonpsychotic children: Risks and implications for mental health services. *Psychiatr Serv* 67:339–341, 2016.
- dosReis S, Tai MH, Goffman D, Lynch SE, Reeves G, Shaw T: Age-related trends in psychotropic medication use among very young children in foster care. *Psychiatr Serv* 65:1452–1457, 2014.
- dosReis S, Zito JM, Safer DJ, Gardner JF, Puccia KB, Owens PL: Multiple psychotropic medication use for youth: A two-state comparison. *J Child Adolesc Psychopharmacol* 15:68–77, 2005.
- dosReis S, Zito JM, Safer DJ, Soeken KL: Mental health services for youth in foster care and disabled youth. *Am J Public Health* 91: 1094–1099, 2001.
- Ford T, Vostanis P, Meltzer H, Goodman R: Psychiatric disorder among British children looked after by local authorities: Comparison with children living in private households. *Br J Psychiatry* 190: 319–325, 2007.
- Furu K, Hjellvik V, Hartz I, Karlstad Ø, Skurtveit S, Blkx HS, Størm H, Selmer RM: Use of Prescription Drugs in Children and Adolescents in Norway 2008–2017 (Report in Norwegian). Oslo, Norway, National Institute of Public Health, 2018.
- Garbe E, Mikolajczyk RT, Banaschewski T, Petermann U, Petermann F, Kraut AA, Langner I: Drug treatment patterns of attention-deficit/hyperactivity disorder in children and adolescents in Germany: Results from a large population-based cohort study. *J Child Adolesc Psychopharmacol* 22:452–458, 2012.
- Garfield LD, Brown DS, Allaire BT, Ross RE, Nicol GE, Raghavan R: Psychotropic drug use among preschool children in the Medicaid program from 36 states. *Am J Public Health* 105:524–529, 2015.
- Garland AF, Hough RL, McCabe KM, Yeh MAY, Wood PA, Aarons GA: Prevalence of psychiatric disorders in youth across five sectors of care. *J Am Acad Child Adolesc Psychiatry* 40:409–418, 2001.
- Gilbert R, Widom CS, Browne K, Fergusson D, Webb E, Janson S: Burden and consequences of child maltreatment in high-income countries. *Lancet* 373:68–81, 2009.
- Giles LL, Martini DR: Challenges and promises of pediatric psychopharmacology. *Acad Pediatr* 16:508–518, 2016.
- Gjerden P, Bramness JG, Tvette IF, Slørdal L: The antipsychotic agent quetiapine is increasingly not used as such: Dispensed prescriptions in Norway 2004–2015. *Eur J Clin Pharmacol* 73:1173–1179, 2017.
- Green JG, McLaughlin KA, Berglund PA, Gruber MJ, Sampson NA, Zaslavsky AM, Kessler RC: Childhood adversities and adult psychiatric disorders in the national comorbidity survey replication I: Associations with first onset of DSM-IV disorders. *Arch Gen Psychiatry* 67:113–123, 2010.
- Hojlund M, Pottegard A, Johnsen E, Kroken RA, Reutfors J, Munk-Jorgensen P, Correll CU: Trends in utilization and dosing of antipsychotic drugs in Scandinavia: Comparison of 2006 and 2016. *Br J Clin Pharmacol* 85:1598–1606, 2019.
- Hunt TKA, Slack KS, Berger LM: Adverse childhood experiences and behavioral problems in middle childhood. *Child Abuse Negl* 67: 391–402, 2017.
- Jozefiak T, Kayed NS, Rimehaug T, Wormdal AK, Brubakk AM, Wichstrom L: Prevalence and comorbidity of mental disorders among adolescents living in residential youth care. *Eur Child Adolesc Psychiatry* 25:33–47, 2016.
- Keast SL, Tidmore LM, Shropshire D, Nesser N, Lambert TL: Characterization of chronic multiclass psychotropic polypharmacy and psychotherapy in foster care youth in a state Medicaid population. *J Manag Care Spec Pharm* 25:1340–1348, 2019.
- Krogh F, Indergård PJ, Solbakken T, Urfjell B: Activity-data for the Children and Adolescents Mental Health Services 2016 (Report in Norwegian). Oslo, The Norwegian Directorate of Health, 2016. Available at: <https://www.helsedirektoratet.no/rapporter/aktivitetsdata-for-psykisk-helsevern-for-barn-og-unge> (accessed July 4, 2020).
- Linares LO, Martinez-Martin N, Castellanos FX: Stimulant and atypical antipsychotic medications for children placed in foster homes. *PLoS One* 8:e54152, 2013.
- Locher C, Kossowsky J, Koechlin H, Lam TL, Barthel J, Berde CB, Gaab J, Schwarzer G, Linde K, Meissner K: Efficacy and safety of selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, and placebo for common psychiatric disorders among children and adolescents: A systematic review and meta-analysis. *JAMA Psychiatry* 74:1011–1020, 2017.
- McLaren JL, Barnett ER, Zayas MTC, Lichtenstein J, Acquilano SC, Schwartz LM, Woloshin S, Drake RE: Psychotropic medications for highly vulnerable children. *Expert Opin Pharmacother* 19:547–560, 2018.
- McMillen JC, Scott LD, Zima BT, Ollie MT, Munson MR, Spitznagel E: Use of mental health services among older youth in foster care. *Psychiatr Serv* 55:811–817, 2004.
- National Institute for Health and Care Excellence: Attention deficit hyperactivity disorder: Diagnosis and management [NG87]. 2018. Available at: <https://www.nice.org.uk/guidance/ng87> (accessed July 7, 2020).
- Nesvag R, Hartz I, Bramness JG, Hjellvik V, Handal M, Skurtveit S: Mental disorder diagnoses among children and adolescents who use antipsychotic drugs. *Eur Neuropsychopharmacol* 26:1412–1418, 2016.
- Oerbeck B, Furu K, Zeiner P, Aase H, Reichborn-Kjennerud T, Pripp AH, Overgaard KR: Child and parental characteristics of medication use for attention-deficit/hyperactivity disorder. *J Child Adolesc Psychopharmacol* 30:456–464, 2020.
- Olfson M, Marcus SC, Weissman MM, Jensen PS: National trends in the use of psychotropic medications by children. *J Am Acad Child Adolesc Psychiatry* 41:514–521, 2002.

- Piovani D, Clavenna A, Bonati M: Prescription prevalence of psychotropic drugs in children and adolescents: An analysis of international data. *Eur J Clin Pharmacol* 75:1333–1346, 2019.
- Pringsheim T, Hirsch L, Gardner D, Gorman DA: The pharmacological management of oppositional behaviour, conduct problems, and aggression in children and adolescents with attention-deficit hyperactivity disorder, oppositional defiant disorder, and conduct disorder: A systematic review and meta-analysis. Part 1: Psychostimulants, alpha-2 agonists, and atomoxetine. *Can J Psychiatry* 60:42–51, 2015.
- Raghavan R, Zima BT, Andersen RM, Leibowitz AA, Schuster MA, Landsverk J: Psychotropic medication use in a national probability sample of children in the child welfare system. *J Child Adolesc Psychopharmacol* 15:97–106, 2005.
- R Development Core Team: *A Language and Environment for Statistical Computing*. Vienna, Austria, R Foundation for Statistical Computing, 2020.
- Rettew DC, Greenblatt J, Kamon J, Neal D, Harder V, Wasserman R, Berry P, MacLean CD, Hogue N, McMains W: Antipsychotic medication prescribing in children enrolled in Medicaid. *Pediatrics* 135:658, 2015.
- Safer DJ, Zito JM, DosReis S: Concomitant psychotropic medication for youth. *Am J Psychiatry* 160:438–449, 2003.
- Steinhausen HC, Bisgaard C: Nationwide time trends in dispensed prescriptions of psychotropic medication for children and adolescents in Denmark. *Acta Psychiatr Scand* 129:221–231, 2014.
- Sultan RS, Correll CU, Schoenbaum M, King M, Walkup JT, Olfson M: National patterns of commonly prescribed psychotropic medications to young people. *J Child Adolesc Psychopharmacol* 28:158–165, 2018.
- Turney K, Wildeman C: Mental and physical health of children in foster care. *Pediatrics* 138:e20161118, 2016.
- Vanderwerker L, Akincigil A, Olfson M, Gerhard T, Neese-Todd S, Crystal S: Foster care, externalizing disorders, and antipsychotic use among Medicaid-enrolled youth. *Psychiatr Serv* 65:1281–1284, 2014.
- Vitiello B: An international perspective on pediatric psychopharmacology. *Int Rev Psychiatry* 20:121–126, 2008.
- World Health Organization (WHO): *Guidelines for ATC Classification and DDD Assignment 2020*. Oslo, Norway, WHO Collaborating Centre for Drug Statistics Methodology, 2020.
- Zhou X, Zhang Y, Furukawa TA, Cuijpers P, Pu J, Weisz JR, Yang L, Hetrick SE, Giovane CD, Cohen D, James AC, Yuan S, Whittington C, Jiang X, Teng T, Cipriani A, Xei P: Different types and acceptability of psychotherapies for acute anxiety disorders in children and adolescents: A network meta-analysis. *JAMA Psychiatry* 76:41–50, 2019.
- Zima BT, Bussing R, Crecelius GM, Kaufman A, Belin TR: Psychotropic medication treatment patterns among school-aged children in foster care. *J Child Adolesc Psychopharmacol* 9:135–147, 1999.
- Zito JM, Pennap D, Safer DJ: Antidepressant use in Medicaid-insured youth: Trends, covariates, and future research needs. *Front Psychiatry* 11:113, 2020.
- Zito JM, Safer DJ, de jong-van den Berg LTW, Janhsen K, Fegert JM, Gardner JF, Gleaske G, Valluri SC: A three-country comparison of psychotropic medication prevalence in youth. *Child Adolesc Psychiatry Ment Health* 2:26, 2008a.
- Zito JM, Safer DJ, Sai D, Gardner JF, Thomas D, Coombes P, Dubowski M, Mendez-Lewis M: Psychotropic medication patterns among youth in foster care. *Pediatrics* 121:e157–e163, 2008b.
- Zito JM, Tobi H, de jong-van den Berg LTW, Fegert JM, Safer DJ, Janhsen K, Hansen DG, Gardner DG, Gleaske G: Antidepressant prevalence for youth: A multi-national comparison. *Pharmacoeconomol Drug Saf* 15:793–798, 2006.

Address correspondence to:

Beate Oerbeck, PhD

Division of Mental Health and Addiction

Oslo University Hospital

PO Box 4959 Nydalen

Oslo 0424

Norway

E-mail: b-oerbe@online.no