

Monitoring of Adverse Drug Reaction-Related Parameters in Children, Youth, and Young Adults Prescribed Antipsychotic Drugs by General Practitioners

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Abstract

Objective: The aim of the study was to assess monitoring of adverse drug reaction (ADR)-related parameters in children, youth, and young adults treated with second-generation antipsychotic drugs (SGAs) prescribed by general practitioners (GPs).

Methods: This retrospective follow-up study included children, youth, and young adults aged 0–24 years, who had an initial prescription of an SGA recorded in the Clinical Practice Research Datalink between 2000 and 2017, and who were prescribed an SGA more than once for a duration of at least 6 months. It included an assessment of which ADR-related physical parameters (weight, height, body-mass index, waist circumference, pulse, blood pressure, and heart examination) and laboratory parameters (glucose, HbA1c, lipids, and prolactin) were monitored in children, youth, and young adults at least once every 6-month period, stratified by sex, age categories, and calendar years.

Results: In total, 7006 patients were included and the mean duration of follow-up was 1.6 years. Monitoring frequencies of all parameters were below 25%. Blood pressure and weight were monitored in 23.6% and 23.4%, respectively, of all children, youth, and young adults during the first half year; waist circumference was monitored in 0.2%. Females were monitored more often than males, some differences between age categories were observed, and monitoring frequencies increased after 2000, but did not exceed 35% in any year.

Conclusion: Monitoring frequencies of ADR-related parameters in children, youth, and young adults treated with SGAs prescribed by a GP were low. Monitoring in primary care should be improved to enable a better evaluation of the benefit–risk balance during antipsychotic drug therapy.

Keywords: adverse effects, antipsychotic agents, youth, drug monitoring, primary health care

Introduction

ANTIPSYCHOTIC DRUGS ARE frequently prescribed to children, youth, and young adults (hereafter referred to as youth) to treat psychiatric disorders, including psychotic symptoms, conduct disorders, irritability associated with autism, and attention-deficit/hyperactivity disorder (Kalverdijk et al. 2017; Pringsheim et al. 2019). Although most often prescribed by psychiatrists, other physicians also have a prominent role in treating youth with antipsychotic drugs (Marston et al. 2014; Burcu et al. 2016; Huskamp et al. 2016; Pringsheim et al. 2019). General practitioners (GPs) can

initiate antipsychotic drug therapy in youth, but prescribing antipsychotics by GPs most often concerns continuation of therapy started by specialists.

Regardless of the specialty of the prescriber, careful evaluation and monitoring of benefits and risks of antipsychotic drugs are especially important in youth since off-label prescribing is common, and this young population is vulnerable (Sohn et al. 2016). Monitoring risks of antipsychotic drugs in the individual youth is important because these drugs can frequently cause severe adverse drug reactions (ADRs), including extrapyramidal, cardiometabolic, and endocrine adverse effects (Correll et al. 2009; Roke et al. 2009;

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De Hert et al. 2011; Pisano et al. 2016; Minjon et al. 2019). Examples of these adverse effects are parkinsonism, weight gain, hypertension, tachycardia, development of diabetes mellitus, and gynecomastia. The safety risks in youth are not the same as in adults (Liu et al. 2019). For example, the extent of weight gain induced by antipsychotic drugs was found to be even greater in youth than in adults (Safer 2004; Kryzhanovskaya et al. 2012). Additionally, gynecomastia can also have a high emotional impact on boys during puberty.

No antipsychotic drug is free of ADRs, and second-generation antipsychotics (SGAs) can cause different ADRs than first-generation antipsychotics. Generally, SGAs have a lower risk of extrapyramidal adverse effects than first-generation antipsychotics, but can cause more metabolic adverse effects (Huhn et al. 2019). In particular, prescribing SGAs in youth requires regular monitoring to detect cardiometabolic adverse effects and prevent harm. Monitoring frequencies in youth treated with antipsychotic drugs have been studied in clinical practice and have appeared to be suboptimal (Ghate et al. 2012; Delate et al. 2014; Edelsohn et al. 2015; Okumura et al. 2018; Hayden et al. 2020), but the degree to which GPs monitor youth treated with antipsychotic drugs is unclear.

Clinical guidelines are available to provide information regarding monitoring and evaluation of ADRs of SGAs. These ADRs can be monitored through related parameters, including physical—weight, height, body-mass index (BMI), waist circumference, pulse, blood pressure, and heart examination—and laboratory—glucose, HbA1c, lipids, and prolactin—parameters. There are differences between guidelines on which parameters they advise to monitor and the frequency of monitoring (American Academy of Child and Adolescent Psychiatry [AACAP] 2011; Pringsheim et al. 2011). In the United Kingdom, the National Institute for Health and Care Excellence (NICE) guideline provides guidance and advice on how to monitor ADR-related parameters in children and young people treated with antipsychotic drugs (National Institute for Health and Care Excellence [NICE] 2016). The NICE guideline is available to all health care providers and advises, for example, monitoring weight at baseline, weekly for the first 6 weeks, at 12 weeks, and every 6 months thereafter. Although most prescribers of antipsychotic drugs to youth are aware of the existence of monitoring guidelines (McLaren et al. 2017), previous studies have illustrated that in daily practice not all youth were monitored (Ghate et al. 2012; Delate et al. 2014; Edelsohn et al. 2015; Okumura et al. 2018; Hayden et al. 2020), and practices varied regarding which parameters require monitoring and how frequently it was done (Minjon et al. 2018).

The aim of this study was to assess monitoring of ADR-related parameters in youth treated with SGAs prescribed by GPs. Additionally, differences in monitoring across sex, age categories, and calendar years were determined.

Methods

Setting

Data for this study were obtained from the Clinical Practice Research Datalink (CPRD), which holds electronic medical records from 674 general practices in the United Kingdom (Herrett et al. 2015). Although not all practices in the United Kingdom participate, the data are representative for the whole population in terms of sex, age, and ethnicity (Herrett et al. 2015). The database provides detailed information on demographics, clinical events, drug prescriptions, referrals, hospital admissions, and tests. Data collection

began in January 1987, and over 11 million persons are currently included (Herrett et al. 2015). Approval for this study was obtained from the CPRD Independent Scientific Advisory Committee, reference number: 17_052R2A.

Study population and design

Youth aged 0–24 years, who had an initial prescription of an SGA (BNF code 04020102; Supplementary Table S1) recorded in the CPRD database between January 2000 and December 2017, and who were prescribed an SGA more than once for a duration of at least 6 months were included. This initial prescription by the GP could be the start of the antipsychotic drug therapy as well as continuation of the treatment started by specialists. Youth were followed from the date of their first prescription of an SGA (index date) until the end of SGA prescriptions, age >24 years, transfer out of the practice, last data collection for the practice, or date of death, whichever came first. Youth needed to have at least 6 months of valid data available before the index date to be included in this study. If they were again prescribed an SGA after the end of follow-up, this second episode was not included.

This was a retrospective follow-up study, and the individual follow-up time for all youth was divided into fixed time frames of 6 months (182 days). The theoretical duration of antipsychotic drug usage was calculated by dividing the amount prescribed by the dosage regimen for each prescription. When the theoretical duration of antipsychotic drug usage was unknown, <1 or >365 days, the overall median duration of a prescription was utilized, which was 28 days for oral medication and 14 days for intramuscular medication. Youth could switch to another type of SGA during follow-up, and the period that youth were treated with SGAs was considered to be continuous if the gap between the theoretical end date of one prescription and the start date of the next prescription was less than 90 days. When the follow-up time of antipsychotic drug usage did not cover the complete final 6-month time frame, this time frame was excluded, and follow-up was censored at the end of the previous time frame.

Outcome and determinants

It was assessed whether youth were monitored for ADR-related parameters at least once during each fixed 6-month time frame based on the NICE guideline, including monitoring of children and young people treated with antipsychotic drugs (CG155) (National Institute for Health and Care Excellence [NICE] 2016). These parameters included both physical—weight, height, BMI, waist circumference, pulse, blood pressure, and heart examination—and laboratory—glucose, HbA1c, lipids, and prolactin—parameters. Monitoring of BMI was included when reported as such in the database and was not included when height and weight were both measured, but BMI was lacking. Code lists of physical and laboratory parameters were composed (Supplementary Table S2) and checked by a second author (E.R.H.).

Differences in monitoring frequencies of ADR-related physical and laboratory parameters were determined across sex, age categories (0–11, 12–18, and 19–24 years old), and calendar years.

Data analyses

Descriptive statistics were used to determine the percentage of youth who had been monitored for physical and laboratory parameters at least once every 6 months when prescribed an SGA. Data were stratified by sex, age categories, and calendar years.

Relative risks (RRs) and 95% confidence intervals (95% CIs) were calculated when comparing strata. Statistical analyses were performed with SAS 9.4.

Results

There were 15,342 youths aged 0–24 years who received an initial prescription of an SGA between 2000 and 2017 and were prescribed an SGA more than once. After excluding youth with less than 6 months of valid data before the index date and a follow-up time of less than 6 months, 7006 youths were included in this study (Table 1). Most were male ($n=4330$; 61.8%), aged 19–24 years ($n=3781$; 54.0%), and were prescribed risperidone at baseline ($n=2932$; 41.8%).

Monitoring of physical and laboratory parameters

During each 6-month time frame, physical parameters were monitored in less than 25% of the youth and laboratory parameters in less than 15% (Fig. 1). Although monitoring frequencies were low across all parameters, the physical parameters monitored most frequently in youth during the first half year that they were prescribed an SGA were blood pressure ($n=1656$; 23.6%) and weight ($n=1640$; 23.4%), and the laboratory parameters monitored most frequently were glucose ($n=937$; 13.4%) and lipids ($n=565$; 8.1%). Least frequently monitored parameters during the first half year were waist circumference ($n=13$; 0.2%) and HbA1c ($n=205$; 2.9%).

The duration of usage differed between youth (mean 1.6 years and median 1.0 year; Table 1), but no prominent differences were observed in monitoring frequencies during the first half year an SGA was prescribed when comparing youth who were prescribed an SGA for <12, 12–24, and ≥ 24 months.

Sex and age

Most parameters were monitored relatively more often in females compared with males during the first half year they were prescribed an SGA (Table 2); regardless, all parameters were monitored in less than 35% of the females. For example, BMI and blood pressure were monitored relatively more often in females than in males (24.5% vs. 12.7%: RR [95% CI]=1.9 [1.7–2.1] and 33.6% vs. 17.5%: RR [95% CI]=1.9 [1.8–2.1], respectively), as were glucose and prolactin (18.0% vs. 10.5%: RR [95% CI]=1.7 [1.5–1.9] and 6.2% vs. 3.6%: RR [95% CI]=1.7 [1.4–2.1], respectively).

Monitoring frequencies during the first half year differed across age categories (Table 2), but remained below 30% for all parameters. Height was monitored relatively more often in children 0–11 and 12–18 years old compared with those 19–24 years old (16.2% vs. 8.7%: RR [95% CI]=1.9 [1.5–2.3] and 14.6% vs. 8.7%: RR [95% CI]=1.7 [1.5–1.9], respectively). None of the children 0–11 years old were monitored for BMI; this was relatively most often monitored in those 19–24 years old (12–18/19–24 years old: 14.9% vs. 21.8%: RR [95% CI]=0.7 [0.6–0.8]).

Calendar years

Monitoring frequencies of all parameters during the first half year that an SGA was prescribed increased compared with the year 2000, but in no year were the physical parameters monitored in more than 35% of the youth or laboratory parameters in more than 20% (Fig. 2). Weight and blood pressure were monitored relatively most frequently when the year of the index date was 2012 ($n=157$;

TABLE 1. CHARACTERISTICS OF THE STUDY POPULATION ($N=7006$)

Characteristic	n (%)
Sex	
Females	2676 (38.2)
Males	4330 (61.8)
Age (at index date; years)	
0–5	29 (0.4)
6–11	657 (9.4)
12–18	2539 (36.2)
19–24	3781 (54.0)
Year of index date	
2000–2005	1618 (23.1)
2006–2011	2706 (38.6)
2012–2017	2682 (38.3)
Duration of second-generation antipsychotic drug use^a (months)	
<12	2828 (40.4)
12–24	2199 (31.4)
≥ 24	1979 (28.2)
Second-generation antipsychotic drug (at index date)^b	
Risperidone	2932 (41.8)
Quetiapine	1742 (24.9)
Olanzapine	1707 (24.4)
Aripiprazole	528 (7.5)
Other	115 (1.6)
Disorders (ever before the index date)^c	
Psychiatric disorders	
Depression	2649 (37.8)
Anxiety disorder	1927 (27.5)
Psychotic disorder	1282 (18.3)
Sleep disorder	1199 (17.1)
Attention-deficit/hyperactivity disorder	968 (13.8)
Autism spectrum disorder	920 (13.1)
Eating disorder	396 (5.7)
Bipolar disorder	239 (3.4)
Somatic disorders	
Overweight	204 (2.9)
Diabetes mellitus	45 (0.6)
Dyslipidemia	4 (0.1)
Drug use (half year before the index date)^c	
Cardiovascular	
Antidiabetics (not insulin)	22 (0.3)
Antilipemics	7 (0.1)
Insulins	30 (0.4)
Central nervous system	
Antidepressants	2801 (40.0)
Antipsychotics (excl. second-generation antipsychotics)	416 (5.9)
Anxiolytics/hypnotics/benzodiazepines	1763 (25.2)
Mood stabilizers	382 (5.5)
Stimulants	592 (8.4)

Index date: initial prescription of a second-generation antipsychotic drug in the CPRD database.

^aTotal duration of follow-up (years): mean 1.6 and median 1.0.

^bEighteen children, youth, and young adults were prescribed two types of second-generation antipsychotic drugs ($n=7024$).

^cSeveral children, youth, and young adults had more than one disorder and used multiple drugs ($n>7006$). The disorders and drugs mentioned were a selection of those included in the CPRD database; children, youth, and young adults could also have other disorders and use other drugs not shown in this table.

CPRD, Clinical Practice Research Datalink.

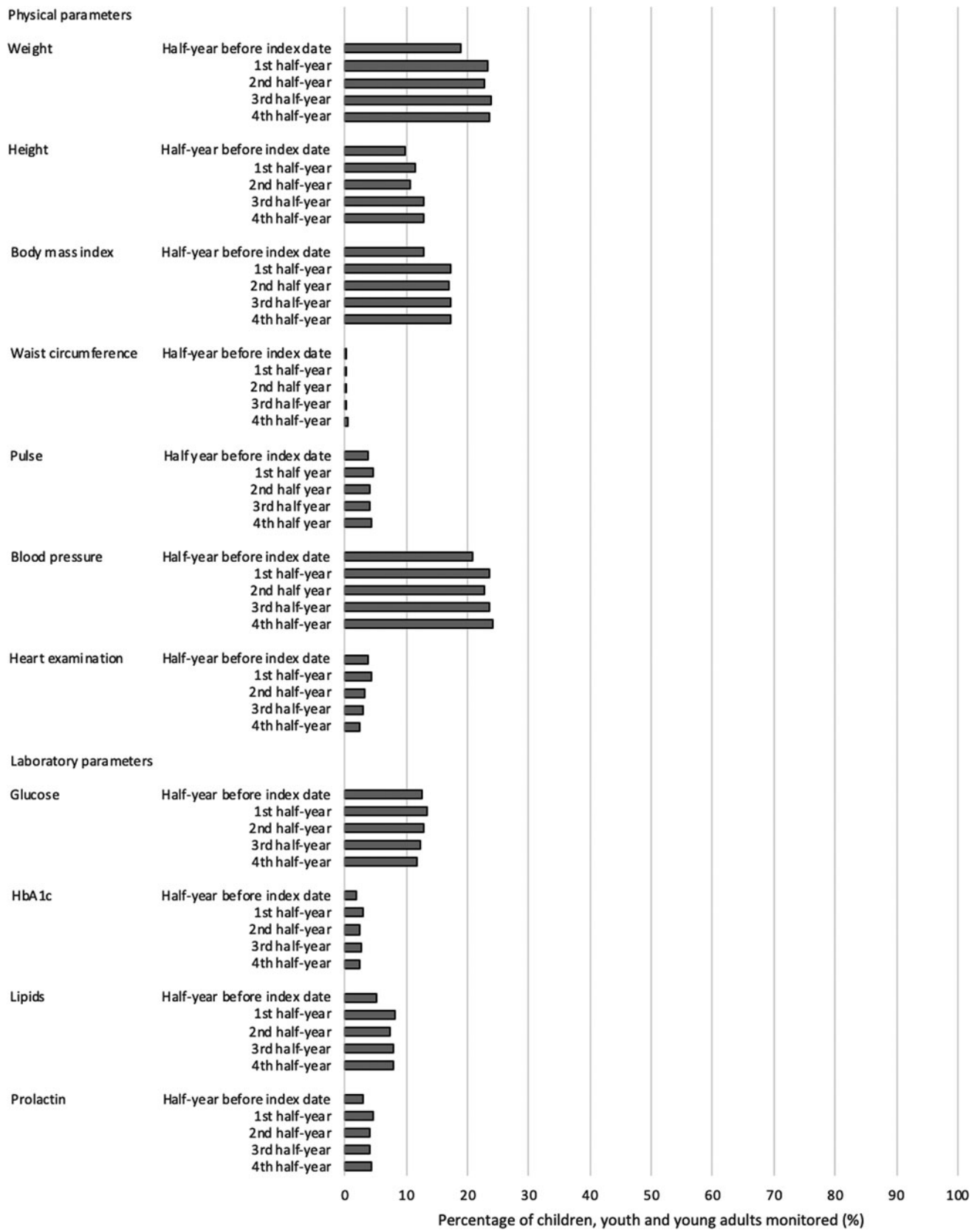


FIG. 1. Monitoring of ADR-related parameters in children, youth, and young adults treated with second-generation antipsychotic drugs prescribed by GPs. Total number of children, youth, and young adults: half year before the index date and 1st half year $n = 7006$; 2nd half year $n = 4178$; 3rd half year $n = 2770$; and 4th half year $n = 1979$. ADR, adverse drug reaction; GPs, general practitioners.

TABLE 2. MONITORING OF ADVERSE DRUG REACTION-RELATED PARAMETERS IN CHILDREN, YOUTH, AND YOUNG ADULTS TREATED WITH SECOND-GENERATION ANTIPSYCHOTIC DRUGS PRESCRIBED BY GENERAL PRACTITIONERS DURING THE FIRST HALF YEAR: STRATIFIED BY SEX AND AGE

	Total		Sex		Age (years old)				
	n=7006	Male	Female	Female/male	0–11	12–18	19–24	0–11/19–24	12–18/19–24
		n=4330	n=2676		n=686	n=2539	n=3781		
	%	%	%	RR [95%CI]	%	%	%	RR [95%CI]	RR [95%CI]
Physical parameters									
Weight	23.4	19.3	30.0	1.6 [1.4–1.7]	19.7	23.9	23.8	0.8 [0.7–1.0]	1.0 [0.9–1.1]
Height	11.6	11.6	11.5	1.0 [0.9–1.1]	16.2	14.6	8.7	1.9 [1.5–2.3]	1.7 [1.5–1.9]
Body-mass index	17.2	12.7	24.5	1.9 [1.7–2.1]	0	14.9	21.8	—	0.7 [0.6–0.8]
Waist circumference	0.2	0.2	0.2	1.0 [0.3–3.1]	0	0.1	0.3	—	0.4 [0.1–1.6]
Pulse	4.5	3.6	6.0	1.7 [1.4–2.1]	4.7	4.7	4.3	1.1 [0.7–1.6]	1.1 [0.9–1.4]
Blood pressure	23.6	17.5	33.6	1.9 [1.8–2.1]	14.3	22.9	25.8	0.6 [0.5–0.7]	0.9 [0.8–1.0]
Heart examination	4.4	3.9	5.3	1.4 [1.1–1.7]	2.0	5.2	4.4	0.5 [0.3–0.8]	1.2 [1.0–1.5]
Laboratory parameters									
Glucose	13.4	10.5	18.0	1.7 [1.5–1.9]	6.0	13.8	14.4	0.4 [0.3–0.6]	1.0 [0.8–1.1]
HbA1c	2.9	2.3	4.0	1.8 [1.3–2.3]	0.4	3.0	3.4	0.1 [0.0–0.4]	0.9 [0.7–1.2]
Lipids	8.1	7.5	8.9	1.2 [1.0–1.4]	3.9	8.7	8.4	0.5 [0.3–0.7]	1.0 [0.9–1.2]
Prolactin	4.6	3.6	6.2	1.7 [1.4–2.1]	3.9	6.9	3.3	1.2 [0.8–1.8]	2.1 [1.7–2.6]

n: number of children, youth, and young adults.

Bold: significant difference.

RR [95%CI], relative risk [95% confidence interval].

30.3%, and $n = 161$; 31.0%, respectively). Glucose was monitored relatively most frequently when the year of the index date was 2013 ($n = 113$; 20.0%).

Discussion

Monitoring frequencies of ADR-related parameters were low in youth treated with an SGA prescribed by a GP. The physical parameters were monitored in less than 25% of the youth and laboratory parameters in less than 15% in the different 6-month time frames. There were no prominent changes in the percentages of youth monitored during the different 6-month time frames that they were prescribed an SGA. Although monitoring frequencies were low, females were monitored relatively more often than males, and there were some differences between age categories. Monitoring frequencies during the first half year that an SGA was prescribed increased after 2000, but did not exceed 35% in any year, and seemed to flatten over the years.

A study by Rettew et al. (2015) indicated that metabolic monitoring is more likely to occur in children treated by psychiatrists compared with those treated by nonpsychiatrists, although a study by Wakefield et al. (2020) revealed fewer differences in monitoring frequencies between psychiatrists and primary care providers. Previous studies have found different monitoring frequencies in youth, but the present findings—that these frequencies are low—are consistent (Ghate et al. 2012; Delate et al. 2014; Edelson et al. 2015; Okumura et al. 2018; Hayden et al. 2020). A study by Rodday et al. (2015) indicated that nearly all psychiatrists reported routinely monitoring height and weight in children, but waist circumference or an electrocardiogram was reported in less than a quarter of these children. Other studies also illustrated that monitoring frequencies for glucose were higher compared with lipids, but remained suboptimal (Edelson et al. 2015; Hayden et al. 2020).

There were significant differences in monitoring frequencies indicated in this current study across sex and age categories. Previous studies have also shown that age may influence metabolic

monitoring frequencies, as in these studies, older youth were monitored more often than younger children (Morrato et al. 2010b; Raebel et al. 2014). An explanation for this increase in monitoring of laboratory parameters with age could be the fear of needles as it has been shown that this fear is more common in younger children and decreases with increasing age (McLenon and Rogers 2019). Few previous studies have indicated the influence of sex on monitoring, but it seems that females were monitored relatively more often for laboratory parameters than males (Raebel et al. 2014; Edelson et al. 2015), as also shown in this current study.

In the United Kingdom, the NICE guideline CG155 “Psychosis and schizophrenia in children and young people: recognition and management” provides recommendations on baseline investigations and monitoring for children and young people prescribed antipsychotic drugs (National Institute for Health and Care Excellence [NICE] 2016). This guideline was first published in 2013 and last updated in 2016 and recommends monitoring most parameters included in this study at baseline and every 6 months thereafter when an antipsychotic drug is prescribed. It advises that a heart examination (electrocardiogram) should be performed only when there are risk factors present, including a personal or family history of cardiovascular disease. Looking into the results of this study, most youth were not monitored according to the recommendations of this guideline. Although the present study showed that monitoring frequencies have increased since 2000, no prominent increase was observed after introduction of the NICE guideline in 2013. Previous studies have also demonstrated that after the introduction of monitoring recommendations, warnings for ADRs, or interventions, monitoring frequencies may increase, but remain inadequate (Morrato et al. 2010a; Mitchell et al. 2012; Cotes et al. 2017; Kara and Penner 2021; Melamed et al. 2021). One reason for the outcome of this current study could be that GPs were not aware or insufficiently informed about these new guideline recommendations. Therefore, although there are guidelines on how to monitor ADR-related parameters in youth treated with antipsychotic drugs, the majority of these youth remain unmonitored.

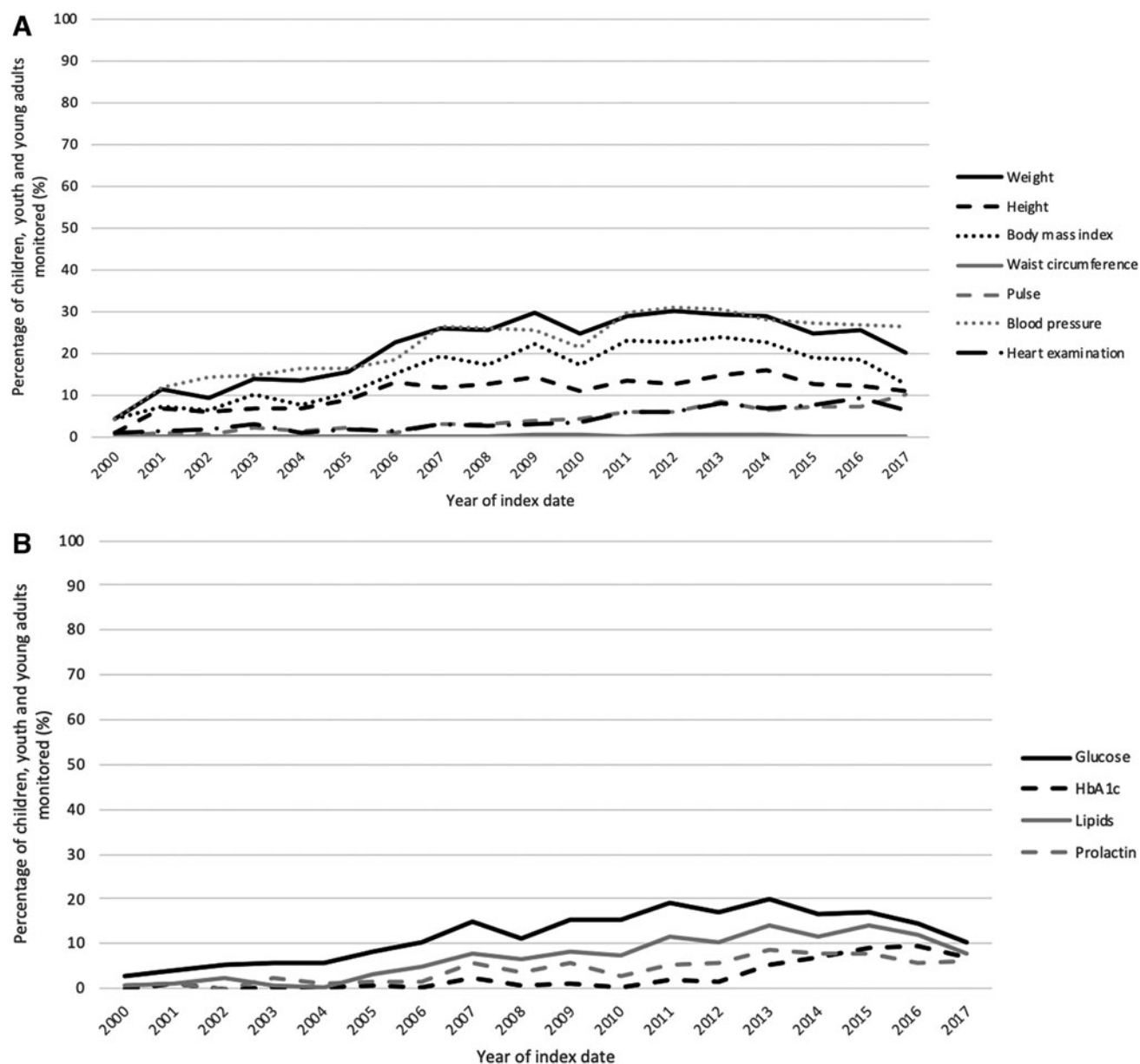


FIG. 2. Monitoring of ADR-related parameters in children, youth, and young adults treated with second-generation antipsychotic drugs prescribed by GPs during the first half year: stratified by calendar year. (A) Monitoring of physical parameters. (B) Monitoring of laboratory parameters. ADR, adverse drug reaction; GPs, general practitioners.

Medical record documentation of the medication and monitoring practices varies between health care professionals (Soto et al. 2002). The quality of documentation can differ as well as the location within the medical record where the information is reported. For this study, monitoring of ADR-related parameters could also have been documented in different parts of the electronic medical records. When searching for monitoring practices within other parts of the medical records included in this study, it was not always clear whether monitoring was previously or currently performed, recommended, or just noted as a point of attention. Therefore, these data were not included in this study. Although this might have led to an underestimation of the monitoring frequencies, this would most likely not lead to considerable differences. Additionally, when data were recorded in different parts of the medical records, this could

lead to unclear medical records, which would also deteriorate monitoring quality in daily clinical practice.

A strength of this study is that the data were drawn from the CPRD, a large, anonymized GP database of high quality and representative of the whole population of the United Kingdom in sex, age, and ethnicity (Herrett et al. 2015). However, this study also has some limitations. Data on monitoring could have been missed if they were not recorded, such as when SGAs were iterated by a GP while the child was monitored by a psychiatrist and results not exchanged, or when data were recorded in an irretrievable part of the medical records, such as free text. Previously, laboratory results were recorded manually, probably resulting in recording only abnormal or confirmatory results. There is no clear date when GP practices switched to laboratory-linked electronic recording. These factors could lead to incomplete or

unclear medical records and therefore underestimated monitoring frequencies. However, these missing data would also negatively influence monitoring quality in daily clinical practice. Finally, it could be that youth were deliberately not monitored, but the considerations and choices made concerning monitoring were not known.

Conclusion

Monitoring frequencies of ADR-related parameters in youth treated with SGAs prescribed by a GP were low. Monitoring in primary care should be improved for the early detection of ADRs and interventions where needed and to enable a better benefit–risk balance during antipsychotic drug therapy.

Clinical Significance

Antipsychotic drugs can cause severe ADRs, which could have a great impact on the quality of life of youth. Therefore, monitoring of these ADRs is important. Nevertheless, this study showed that youth treated with SGAs were monitored infrequently for ADR-related physical and laboratory parameters. Future research should focus on identifying underlying barriers and facilitators for monitoring. These can be barriers involving the prescriber of an SGA, such as a lack of electronic facilitating systems, difficulty in collaborating with other health care professionals, lack of time, or insufficient knowledge about monitoring (Ronsley et al. 2011; Mangurian et al. 2013; Coughlin et al. 2018). A previous study has shown that not all primary care providers were aware of the consensus guidelines (Mangurian et al. 2013). Additionally, psychiatrists and primary care providers seem to have different preferences where monitoring should be performed, and also not all primary care providers share the same opinion (Mangurian et al. 2019), which makes collaboration even more important. The NICE guideline “Autism spectrum disorder in under 19s: support and management” states that antipsychotic drug therapy should be started and monitored by a pediatrician or psychiatrist, and when it is transferred to primary care, the specialist should give clear guidance (National Institute for Health and Care Excellence [NICE] 2013). Barriers can also be related to the patient as parents can forget to obtain a laboratory test and may not see its importance or youth can refuse to take a test because of a fear of needles (McLenon and Rogers 2019).

Regarding facilitators, the use of an electronic medical record system can facilitate monitoring practices as this seems to improve the quality of clinical notes (Burke et al. 2015). Including a reminder system to notify the health care professional about what should be monitored may further enhance monitoring practices. Additionally, shared decision-making may improve monitoring practices. Patients would like guidance and information on ADRs and monitoring of effects (Nederlof et al. 2017; Kaar et al. 2019). For young children, this information could be provided to their caregivers. Health care professionals involved in the antipsychotic drug therapy of youth, including GPs, psychiatrists, and pharmacists, have an important role in providing clear information and guidance. Explaining which effects could be expected and why monitoring is important may create more awareness and compliance to therapy, including monitoring. Investigating and prioritizing the barriers and facilitators could help improve the monitoring frequencies.

Ethical Standards

The study was approved by the Clinical Practice Research Datalink’s Independent Scientific Advisory Committee (reference number 17_052R2A). Data for this study were obtained from CPRD and were received anonymized.

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Disclosures

L.M., M.T.B., A.L., T.C.G.E., and E.R.H. report no financial interests or potential conflicts of interest. E.v.d.B. received a travel reimbursement from Medice to attend an international scientific convention on child and adolescent psychiatry (2017). She reports no financial interests or potential conflicts of interest.

Supplementary Material

Supplementary Table S1
Supplementary Table S2

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