Drug utilisation among Dutch adolescents: a pharmacy prescription records study

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ABSTRACT
Background Studies on adolescent drug use are scarce as most studies do not distinguish between children and adolescents. Therefore, we assessed overall drug use in adolescents.
Methods A retrospective cohort study was conducted using pharmacy dispensing records from 62 community pharmacies in the Netherlands. Dispensing records of the previous 5 years were extracted for adolescents (12–18 years).
Results The study population consisted of 47 421 adolescents who collected at least one medication prescription during adolescence (mean age 15.5±1.8 years; 48.9% males). Half of them collected dermatologicals (46.2% males; 52.3% females), followed by drugs for the respiratory system (43.4% males; 40.3% females) and anti-infectives for systemic use (31.3% males; 39.1% females). The percentage of males using dermatologicals slightly increased, while the percentage of female users decreased with age. The most prescribed active ingredient was methylphenidate.
Conclusions These insights into adolescent drug use help us to better understand adolescent healthcare use.
Trial registration number Dutch trial register NTR5061.

What is already known?

► Most paediatric drug utilisation studies focus on children or do not distinguish between children and adolescents.
► Drug utilisation among adolescents is important to better understand adolescents' healthcare utilisation and needs.

What this study adds?

► More than half of the adolescents collected prescriptions, with the highest prevalence rates for dermatologicals, drugs for the respiratory system and anti-infectives for systemic use.
► Almost half of the adolescent females collected drugs for the genitourinary system and sex hormones, including oral anticonceptives.
► The largest number of collected prescriptions by adolescents was for methylphenidate.

INTRODUCTION

Studies on drug use among adolescents are scarce. Many drug utilisation studies do not distinguish between children and adolescents,[1] while adolescence is an interesting life phase: children start making their own choices, become responsible for their medication regimen and drug use increases during this period.[2–5]

It is important to know what kind of medication is used by adolescents to get a better understanding of adolescents' healthcare utilisation and needs. Therefore, we aimed to assess overall drug use among adolescents aged 12–18 years, with a focus on different ages and sexes.

METHODS
Study design and data collection
We conducted a retrospective cohort study using pharmacy dispensing records. Data were obtained from Dutch community pharmacies as part of the ADolescent Adherence Patient Tool study,[6] approved by the Medical Review Ethics Committee of the University Medical Centre Utrecht (NL50997.041.14) and registered at the Dutch Trial Register (NTR5061). Dispensing records of the previous 5 years were extracted from adolescents aged 12–18 years at the time of inclusion (between July 2015 and May 2016). These records contained information on date of birth, sex, drug name, amount, dosage, prescription date, and Anatomical Therapeutic Chemical (ATC) classification codes.[7] Personal data, such as name and address, were not extracted, ensuring privacy of individuals.

Database
Duplicates, records with administrative errors and prescriptions for non-medications such as dressing materials were excluded. Moreover, prescriptions collected before the age of 12 were excluded. We divided the ATC codes into five levels to create an overview: anatomical main group, therapeutic subgroup, pharmacological subgroup, chemical subgroup and chemical substance.[7]

Analysis
Microsoft Excel 2010 and Microsoft Access were used for data management. Statistical analyses were performed using IBM SPSS for Windows, V.23.0. First, we calculated descriptive statistics. For skewed data, the median with IQR is shown instead of the mean with SD. Thereafter, non-parametric Mann-Whitney and Kruskal-Wallis tests were used to compare differences between gender and age groups. P values <0.05 were considered statistically significant.

RESULTS

In total, 79 398 adolescents were registered at 62 pharmacies. At the time of inclusion, 58 923 patients (74.2%) collected at least one medication prescription in the previous 5 years. We excluded 10 465 patients who only had a prescription before the age of 12 years, and 1037 patients who only collected non-medications (eg, dressing materials). Therefore, our final study population consisted of 47 421 adolescents (59.7% of total) who collected at least one medication prescription during adolescence. Their mean age was 15.5±1.8 years and 48.9% (n=23 170) were males.

The total number of collected prescriptions was 539 096, and the median number of collected prescriptions per person was 5 (IQR 11) during an average period of 2.7±1.7 years. The individual adolescents received prescriptions for medications within 1–12 ATC groups (median 2; IQR 3). The highest number of prescriptions were for the nervous system, respiratory system and dermatologicals, and the most collected active pharmaceutical ingredient was methylphenidate, that is, 72 077 prescriptions (table 1). Females mostly collected drugs for the genitourinary system and sex hormones, followed by dermatologicals and medicines for the respiratory system.

When looking at the prevalence rates (table 2), half of the study population collected at least one prescription for dermatologicals. Medication prescriptions for the respiratory system and anti-infectives for systemic use were also collected by many adolescents. The most collected number of prescriptions within dermatological preparations (D07) were for triamcinolone (D07AB09; 25.1%) and for hydrocortisone (D07AA02; 20.8%). Most collected prescriptions for obstructive airway diseases (R03) were salbutamol (R03AC02; 45.6%) and fluticasone (R03BA05; 22.2%). Desloratadine (R06AX27; 51.6%) and levocetirizine (R06AE09; 26.0%) were the most collected (third-generation) antihistamines for systemic use (R06). Within antibacterials for systemic use (J01), amoxicillin (J01CA04; 19.8%), nitrofurantoin (J01XE01; 13.5%) and doxycycline (J01AA02; 12.8%) were mostly collected.

One-third of the adolescents collected prescriptions for the alimentary tract and metabolism (table 2), which were mostly prescriptions for sodium fluoride (A01AA01; 21.7%) or macrogol combinations as laxatives (A06AD65; 12.3%). The prescriptions for the nervous system were mainly for methylphenidate (N06BA04; 53.0%) or melatonin (N05CH01; 10.7%).

Almost half of the adolescent females collected drugs for the genitourinary system and sex hormones (table 2), which increased over time from 7% to 73% (age 12–18 years). These prescriptions were almost all for levonorgestrel ethinylestradiol (G03AA07; 76.8%). Only 1% of the males collected drugs for the genitourinary system and sex hormones.

The percentage of females collecting at least one prescription was significantly higher than males for nearly all medicine groups, except for the respiratory system, nervous system and systemic hormonal preparations, excluding sex hormones and insulins (table 2). There was no significant difference between the percentage of males and females collecting at least one prescriptions for sensory organs (p=0.83).

Figure 1 shows the percentage of males and females collecting at least one prescription within the ATC groups (prevalence) per age. The percentage of adolescents collecting drugs for the alimentary tract and metabolism, nervous system, respiratory system and sensory organs decreased during adolescence, whereas adolescents collecting prescriptions for anti-infectives for systemic use and drugs for the musculoskeletal system increased over time (nervous system p=0.02; others p=0.00). The male users of dermatologicals slightly increased, whereas

Table 1 The most collected prescriptions per Anatomical Therapeutic Chemical (ATC) group, sorted from most to least, with the most relevant prescriptions per group

Name	ATC	Prescriptions (N=5 39 096)	
		n	%
Nervous system	N	1 36 085	25.2
Methylphenidate	N06BA04	72 077	13.4
Atomoxetine	N06BA09	3657	0.7
Risperidone	N05A×08	8184	1.5
Melatonin	N05CH01	14 620	2.7
Aripiprazole	N05A×12	3322	0.6
Respiratory system	R	1 05 508	19.6
Desloratadine	R06A×27	17 739	3.3
Levocetirizine	R06AE09	8936	1.7
Salbutamol	R03AC02	16 741	3.1
Fluticasone (glucocorticoids, inhalants)	R03BA05	8143	1.5
Fluticasone (corticosteroids, topical use, nasal)	R01AD08	7473	1.4
Dermatologicals	D	89 003	16.5
Other emollients and protectives	D02AX	11 054	2.1
Fusidic acid	D06A×01	7104	1.3
Triamcinolone	D07AB09	6501	1.2
Hydrocortisone	D07AA02	5379	1.0
Erythromycin	D10AF02	5307	1.0
Genitourinary system and sex hormones	G	53 474	9.9
Levonorgestrel and ethinylestradiol	G03AA07	38 767	7.2
Alimentary tract and metabolism	A	52 232	9.7
Sodium fluoride	A01AA01	11 334	2.1
Macrogol, combinations	A06AD65	6414	1.2
Macrogol	A06AD15	4087	0.8
Cholecalciferol	A11CC05	4574	0.8
Omeprazole	A02BC01	3620	0.7
Anti-infectives for systemic use	J	37 837	7.0
Amoxicillin	J01CA04	6631	1.2
Amoxicillin and beta-lactamase inhibitor	J01CR02	3889	0.7
Nitrofurantoin	J01XE01	4512	0.8
Doxycycline	J01AA02	4267	0.8
Azithromycin	J01FA10	3493	0.6
Sensory organs	S	23 066	4.3
Levocabastine	S01G×02	5282	1.0
Musculoskeletal system	M	17 656	3.3
Diclofenac	M01AB05	6751	1.3
Ibuprofen	M01AE01	5226	1.0
Naproxen	M01AE02	3912	0.7
Systemic hormonal preparations, excluding sex hormones and insulins	H	8584	1.6
Levothyroxine sodium	H03AA01	2836	0.5
Desmopressin	H01BA02	1848	0.3
Prednisolone	H02AB06	1665	0.3
Cardiovascular system	C	5019	0.9
Propranolol	C07AA05	1226	0.2
Blood and blood-forming organs	B	4970	0.9
Ferrous fumarate	B03AA02	1925	0.4
Antiparasitic products, insecticides and repellents	P	3463	0.6
Antineoplastic and immunomodulating agents	L	2199	0.4

the percentage of females users decreased during adolescence (p=0.00; figure 1). Some user percentages did not change over time, such as females using systemic hormonal preparations,

Table 2 Prevalence rates (sorted from most to least) and number of prescriptions per person per Anatomical Therapeutic Chemical (ATC) (sub) group

| ATC (sub)group | Users† (N=47 421) | | No of prescriptions per person | | Users per gender† | | | | |
| | | | | | Females (N=24 251) | | Males (N=23 170) | | |
	n	%	Median	IQR	N	%	N	%	P values
D Dermatologicals	23 396	49.3	2	3	12 691	52.3	10 705	46.2	0.000*
Corticosteroids, dermatological preparations (D07)	11 195	23.6	1	1	6239	25.7	4956	21.4	0.000*
Emollients and protectives (D02)	6559	13.8	1	1	3682	15.2	2877	12.4	0.000*
Anti-acne preparations (D10)	5217	11.0	2	4	3032	12.5	2185	9.4	0.000*
R Respiratory system	19 810	41.8	2	5	9762	40.3	10 048	43.4	0.000*
Antihistamines for systemic use (R06)	9863	20.8	2	3	4804	19.8	5059	21.8	0.000*
Drugs for obstructive airway diseases (R03)	6349	13.4	3	5	3006	12.4	3.343	14.4	0.000*
J Anti-infectives for systemic use	16 753	35.3	1	1	9493	39.1	7260	31.3	0.000*
Antibacterials for systemic use (J01)	15 565	32.8	1	1	8842	36.5	6723	29.0	0.000*
A Alimentary tract and metabolism	15 446	32.6	2	2	8601	35.5	6845	29.5	0.000*
Stomatological preparations (A01)	7431	15.7	1	1	3915	16.1	3516	15.2	0.004*
Laxatives (A06)	4572	9.6	2	2	2805	11.6	1767	7.6	0.000*
N Nervous system	11 639	24.5	3	12	5207	21.5	6432	27.8	0.000*
Psychoanaleptics (N06)	5500	11.6	9	16	1726	7.1	3774	16.3	0.000*
Psycholeptics (N05)	3927	8.3	3	8	1719	7.1	2208	9.5	0.000*
G Genitourinary system and sex hormones	10 952	23.1	4	5	10 742	44.3	210	0.9	0.000*
Sex hormones and modulators of the genital system (G03)	10 509	22.2	4	5	10 428	43.0	81	0.4	0.000*
S Sensory organs	9794	20.7	1	1	4999	20.6	4795	20.7	0.827
Ophthalmologicals (S01)	6806	14.4	1	1	3479	14.4	3327	14.4	0.967
M Musculoskeletal system	9226	19.5	1	1	5618	23.2	3608	15.6	0.000*
Anti-inflammatory and antirheumatic products (M01)	9091	19.2	1	1	5561	22.9	3530	15.2	0.000*
P Antiparasitic products, insecticides and repellents	2566	5.4	1	0	1417	5.8	1149	5.0	0.000*
Antiprotozoals (P01)	1452	3.1	1	0	869	3.6	583	2.5	0.000*
H Systemic hormonal preparations, excluding sex hormones and insulins	1835	3.9	2	3	877	3.6	958	4.1	0.003*
Corticosteroids for systemic use (H02)	967	2.0	1	1	506	2.1	461	2.0	0.456
B Blood and blood-forming organs	1630	3.4	2	2	1151	4.8	479	2.1	0.000*
Antianaemic preparations (B03)	1213	2.6	2	2	915	3.8	298	1.3	0.000*
C Cardiovascular system	1382	2.9	1	2	795	3.3	587	2.5	0.000*
Beta-blocking agents (C07)	620	1.3	1	2	409	1.7	211	0.9	0.000*
L Antineoplastic and immunomodulating agents	245	0.5	4	10	141	0.6	104	0.5	0.044*
Immunosuppressants (L04)	140	0.3	7	11	79	0.3	61	0.3	0.210

*P<0.05.

†User was defined as an adolescent who collected at least one prescription within the ATC (sub)group.

excluding sex hormones and insulins (p=0.26) and antiparasitic products, insecticides and repellents (p=0.14). For males, the percentage using blood and blood-forming organs stayed the same (p=0.69). For both genders, the use of antineoplastic and immunomodulating agents did not change over time (p=0.19 males; p=0.14 females).

DISCUSSION

We provided a comprehensive overview of drug utilisation in adolescents, showing that most adolescents collected at least one prescription for dermatologicals, drugs for the respiratory system or anti-infectives for systemic use. Our data suggest that eczema/acne, allergic rhinitis/asthma and systemic infections are most common among adolescent medication users. The highest number of collected prescriptions was for methylphenidate, while levonorgestrel ethinylestradiol was mostly collected among adolescent females.

A previous study using integrated primary care information (ie, medical records from the period 2000–2005) showed similar results. However, this study showed the highest prevalence rate for anti-infectives, levonorgestrel was the most used drug, and drugs for the nervous system were less commonly used compared with our results.[8] In our study, we used pharmacy prescription records, which provides a reliable overview of drugs that are actually collected by the patient. In addition, the use of methylphenidate increased the last years, which might explain the difference.[9] Another study, focusing on 15-year-old adolescents, reported that anti-inflammatory drugs, analgesics and systemic antihistamines were mostly used.[4 10] However, these results were based on self-reported use for a period of 4 weeks, while the average follow-up time in our study was almost 3 years.

The current study results are based on a large sample (n=47 421) and therefore provides a valuable and updated overview of drug utilisation among adolescents compared with previous studies. Our database contained prescription data from all adolescents registered at 62 community pharmacies,
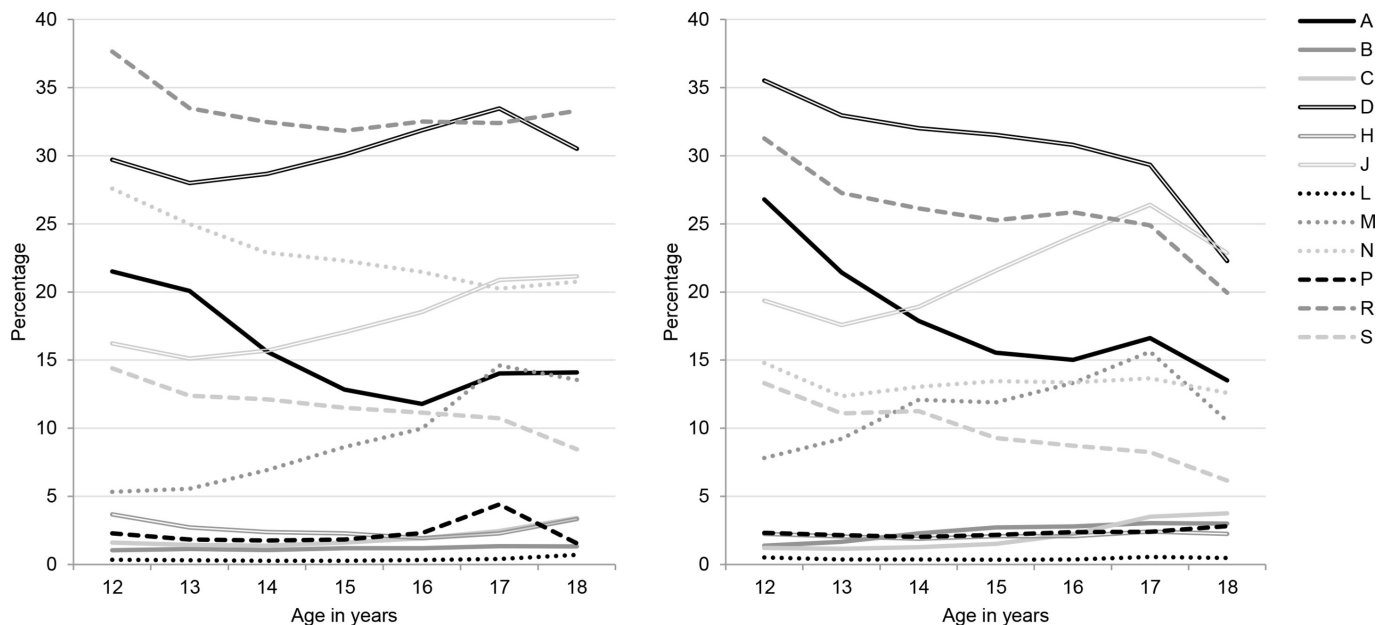
Figure 1 Percentage of males (left) and females (right) collecting one or more prescriptions within the anatomical main group over the years. Prescriptions for 'genitourinary system and sex hormones' are not shown, as those were mostly contraceptives. A, Alimentary tract and metabolism; B, Blood and blood-forming organs; C, Cardiovascular system; D, Dermatologicals; H, Systemic hormonal preparations, excluding sex hormones and insulins; J, Anti-infectives for systemic use; L, Antineoplastic and immunomodulating agents; M, Musculoskeletal system; N, Nervous system; P, Antiparasitic products, insecticides and repellents; R, Respiratory system; S, Sensory organs.

which is roughly 3% out of 1994 community pharmacies operating in the Netherlands in 2017.[11] Dutch patients are generally registered at a single community pharmacy and usually fills all their prescriptions in this pharmacy. Pharmacy prescription records give therefore a complete medication overview and there is no desirability bias, as results are not based on self-report. However, our results might be an overestimation of drug use, because collecting a prescription does not necessarily mean using the drug.[12]

A limitation is the lack of indication for use, which is not included in pharmacy prescription records. However, drug use may be a good indicator for the underlying disease.

The aim of this short report was to provide a comprehensive and updated overview of drug use among adolescents. Most adolescents collected at least one prescription for dermatologicals, drugs for the respiratory system and anti-infectives for systemic use. Future research should focus on adolescents who collect most prescriptions to create a better understanding of adolescent healthcare use and their needs.

REFERENCES
1. Sequi M, Campi R, Clavenna A, *et al*. Methods in pharmacoepidemiology: a review of statistical analyses and data reporting in pediatric drug utilization studies. *Eur J Clin Pharmacol* 2013;69:599–604.
2. Patton GC, Viner R. Pubertal transitions in health. *Lancet* 2007;369:1130–9.
3. Schirm E, van den Berg P, Gebben H, *et al*. Drug use of children in the community assessed through pharmacy dispensing data. *Br J Clin Pharmacol* 2000;50:473–8.
4. Italia S, Brüske I, Heinrich J, *et al*. A longitudinal comparison of drug use among 10-year-old children and 15-year-old adolescents from the German GINIplus and LISAplus birth cohorts. *Eur J Clin Pharmacol* 2016;72:301–10.
5. Murray ML, de Vries CS, Wong IC. A drug utilisation study of antidepressants in children and adolescents using the General Practice Research Database. *Arch Dis Child* 2004;89:1098–102.
6. Kosse RC, Bouvy ML, de Vries TW, *et al*. mHealth intervention to support asthma self-management in adolescents: the ADAPT study. *Patient Prefer Adherence* 2017;11:571–7.
7. WHO Collaborating Centre for Drug Statistics Methodology. *Guidelines for ATC classification and DDD assignment*. 20th edition. Oslo: Norwegian Institute of Public Health, 2017.
8. Sturkenboom MC, Verhamme KM, Nicolosi A, *et al*. Drug use in children: cohort study in three European countries. *BMJ* 2008;337:a2245.
9. National Health Care Institute. The Drug Information System (GIPdatabank). https://www.gipdatabank.nl (accessed 09 Apr 2018).
10. Italia S, Brand H, Heinrich J, *et al*. Utilization of self-medication and prescription drugs among 15-year-old children from the German GINIplus birth cohort. *Pharmacoepidemiol Drug Saf* 2015;24:1133–43.
11. Foundation for Pharmaceutical Statistics (SFK). Data en feiten 2017. 2017. https://www.sfk.nl/publicaties/data-en-feiten/data-en-feiten-2017 (accessed 09 Apr 2018).
12. Mulder B, Groenhof F, Kocabas LI, *et al*. Identification of Dutch children diagnosed with atopic diseases using prescription data: a validation study. *Eur J Clin Pharmacol* 2016;72:73–82.