Prescribing of methylphenidate to children and adolescents in South Africa: A pharmacoepidemiological investigation

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Abstract

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Background: Pharmacoepidemiological studies on ADHD are limited in South Africa. The primary aim was to analyse the prescribing of methylphenidate to patients aged 18 years and younger in the private health care sector.

Methods: Data for a one-month period in 2004 were obtained from a large medical aid administrator. Data were retrospectively analysed. The total database contained medicine records for 355 998 patients.

Results: A total of 66 450 medicine items were prescribed to 34 733 patients aged 18 years and younger. A total of 1 028 patients received prescriptions for methylphenidate. Nearly 3% of children and adolescents therefore received prescriptions for methylphenidate. The average age of these patients was 10.87 (SD = 2.79) years. Most of these prescriptions (63.14%) were for children between seven and twelve years of age. Most prescriptions were for long-acting methylphenidate in 20 mg, 30 mg and 40 mg capsules (48.87%). The average prescribed daily dose (PDD) for methylphenidate was 19.27 (SD = 11.87) mg. The most popular average PDD was 20 mg (42.63% of all methylphenidate prescriptions). The highest average percentage of methylphenidate prescriptions was in the Western Cape (2.58%), and the lowest in the Northern Cape (0.63%).

Conclusions: Numerous claims are being made that methylphenidate is overused or even abused, especially in children of school-going age. Most prescriptions were issued in metropolitan areas in this study, but overuse could not be established. This study was a preliminary study that can lead to more comprehensive studies in future.

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Background to the study

Methylphenidate is the psychostimulant that is most frequently prescribed in the management of Attention Deficit/Hyperactivity Disorder (ADHD) and is also considered to be the first-line medication for the treatment of ADHD.[1,2] ADHD is the most common neurodevelopmental disorder of childhood.[1,3] ADHD also has the distinction of being both the most extensively studied childhood mental disorder and the most controversial.

Recently, the extensive use or overuse of stimulant medication has been a widely publicised concern[1,4-7] and may be due, in part, to the lack of application of definitive diagnostic criteria and the non-specific nature of treatments.[8] Marked increases in prescription rates of psychostimulants, especially methylphenidate, have also resulted in public health concerns about the frequency and appropriateness with which these medications are prescribed. The increase in prescription can partly be accounted for by the lengthening of the duration of treatment into adulthood, and increased treatment among girls. Epidemiologists have also stated that whether a child gets methylphenidate or an equivalent drug depends to a great deal on where he or she lives.[9] The United States of America consumed 85% of Ritalin® (methylphenidate) produced in 1999, with striking variations between states and also between counties.[10] Factors such as economic situation, geographic location and racial background have been shown to play a role in whether a child will receive methylphenidate or not.[3,9,11]

It is generally accepted that ADHD affects 3 to 5% of all school-aged children.[2] Epidemiological data on ADHD and methylphenidate prescribing in South Africa is scarce. This study was an attempt to investigate the prescribing of methylphenidate in the nine provinces (different geographical regions) of South Africa using the claims database of one of the three largest medical aid scheme administrators in South Africa. The primary aim of the study was to analyse and compare the prescribing of methylphenidate to patients aged 18 years and younger in the private health care sector in South Africa.

Methodology

A retrospective, exposure cohort drug utilisation study was conducted. Data (computerised prescription records) for a one-month period in 2004 were obtained from one of the three largest medical aid scheme administrators serving various private medical aid schemes in South Africa and were analysed. The total database contained medicine records for 355 998 patients who claimed one or more prescription items during the month. The medical aid administrator administers data for a variety of medical aids (including closed and open schemes), providing different packages to their members (saving schemes, over-the-counter medicine options and chronic programmes).

All prescription records for methylphenidate were extracted from the database and analysed. Records contained information on the age of the patient, the date of the prescription, the province and the area of residence of the patient, detailed information on the dispensed drug (name, package size, formulation, strength and quantity) and price. The Monthly Index of Medical Specialities (MIMS)[12] and the South African Medicines Formulary[13] were used to classify drugs. All costs in the study are indicated in South African rand (R). One US dollar ($1.00) was equal to R6.21, one British pound (£1.00) was equal to R11.26, and one euro (€1.00) was equal to R7.57 on 30 June 2004. Ethical approval for the study was granted by the Faculty of Health Sciences Research, Technology and Innovation Committee of the Nelson Mandela Metropolitan University. The study adhered to ethical principles and patient confidentiality was maintained. No patient in the study could be identified or traced.

Limitations of the study were the absence of gender and clinical information in the database. Information about over-the-counter medication that patients used was also not included in the database and was therefore not analysed. Although the study may not necessarily be representative of prescription patterns in the entire private health care sector in South Africa, it does provide insight into the prescription of methylphenidate to patients of 18 years and younger, which can provide baseline information for more comprehensive studies in the future.

The focus of this study was only on the prescribing patterns of methylphenidate. It must be noted that a new non-stimulant product for ADHD, atomoxetine, has since been introduced onto the South African market. Generic equivalents for methylphenidate have also become available. These products were, however, not yet available on the market at the time of this study and could therefore not be included in the analysis.

Results and discussion

General prescribing patterns and demographic information of patient population

A total of 66 450 medicine items at a cost of R7 215 193 were prescribed to 34 733 patients aged 18 years and younger during the one-month period in 2004. The average cost per patient was R207.73 for the month, and the average cost per item was R108.58.

Nervous system drugs (under which methylphenidate is classified, Anatomical Therapeutic Chemical (ATC) classification N06BA04[13,14] accounted for 10.41% of the total number of medicine items and 12.85% of the total cost of medicine prescribed to patients of 18 years and younger. Most medicine items (84.34%) were prescribed on an acute basis to these children (all therapeutic categories).

Nearly 3% (2.96%) of children and adolescents (18 years and younger) who had a prescription filled in the one-month period in 2004 had a prescription filled for at least one dose of a methylphenidate-containing product (1 028 patients of the 34 733 patients). A total of 1 028 patients of 18 years and younger were therefore prescribed methylphenidate. This proportional contribution of methylphenidate to all medicines prescribed for children and adolescents in this age group is one measure of utilisation, but is a poor measure of prevalence since it ignores the contribution to the denominator of very young children, in whom ADHD cannot be diagnosed. The age distribution, including prescribing frequency and cost, of all beneficiaries administered aged 18 years and younger who filled a prescription in the one-month period is given in Table I.

Table I: Age distribution of all beneficiaries aged 18 years and younger who filled a prescription in the one-month period

AGE (in years)	NUMBER OF PATIENTS	NUMBER OF ITEMS	COST (in rand)
0	683	1 335	R116 701.98
1	3 056	6 167	R497 887.61
2	2 844	5 582	R481 328.11
3	3 172	6 146	R616 876.92
4	2 193	4 230	R384 539.08
5	1 961	3 783	R367 721.49
6	1 882	3 552	R341 973.31
7	1 665	3 069	R325 034.33
8	1 677	3 163	R357 913.52
9	1 557	2 897	R340 179.61
10	1 600	2 978	R365 669.13
11	1 431	2 731	R350 968.32
12	1 461	2 657	R338 941.60
13	1 441	2 733	R308 944.97
14	1 353	2 626	R320 923.86
15	1 547	3 052	R393 559.31
16	1 666	3 151	R407 663.71
17	1 757	3 274	R439 619.15
18	1 787	3 279	R458 747.18
TOTAL	**34 733**	**66 450**	**R7 215 193.19**

The average age of children and adolescents who received one or more methylphenidate-containing product was 10.87 (SD = 2.79) years. The youngest patient was 0.67 years, the oldest patient was 18.36 years, and the median age was 10.51 years. Most of the children (63.14%) were between seven and twelve years of age (see Table II). Of the total population of children and adolescents in the study, 27.04% (9 391 of the 34 733 patients) were between seven and twelve years of age. This finding is in agreement with that of another South African study[15] conducted in Tshwane in which it was also found that primary school children (aged six to twelve years) received the highest percentage (61%) of methylphenidate prescriptions.

Table II: Age distribution of patients prescribed methylphenidate

AGE GROUP (in years)	FREQUENCY	
	NUMBER	PERCENTAGE
0–6	50	4.86
7–12	649	63.14
13–18	329	32.00
TOTAL	**1 028**	**100.00**

Prescribing frequency of methylphenidate

A total of 1 028 patients received 1 201 prescriptions for methylphenidate during the month. Two factors can be responsible for this finding. Firstly, not all patients received a full month's supply of methylphenidate and it is possible that they may have received a second prescription for the month. Secondly, patients who go away on holiday often fill their prescriptions before the end of the month. In this case, two prescriptions will be claimed in the same month.

Methylphenidate is not indicated (not recommended) for children six years and younger.[12,13] Specialist assessment prior to initiation is required, if possible.[13] It was not possible in this study to determine whether methylphenidate was initiated by a general practitioner or a specialist. In this study, 4.86% of the patients who were prescribed methylphenidate (see Table II) were six years or younger. Most of these patients received prescriptions for methylphenidate 10 mg in a quantity of 30 tablets (that is, 10 mg methylphenidate per day). This is an indication of the off-label use of methylphenidate.

The specific trade names of methylphenidate that were prescribed are indicated in Table III. Ritalin® 10 mg tablets were the most frequently prescribed, followed by Ritalin LA® 20 mg capsules. The modified-release (MR) forms of methylphenidate (Ritalin LA®) accounted for 48.87% of total methylphenidate prescribing. According to the Scottish Health Statistics, MR forms of methylphenidate accounted for 54.9% of all methylphenidate prescribing in Scotland in 2006,[16] which is roughly in agreement with the findings of this study. Another dosage form of methylphenidate (methylphenidate extended-release 18 mg, 36 mg and 54 mg capsules, Concerta®) has since been introduced onto the South African market.

Table III: Prescribing frequency of methylphenidate trade name products

TRADE NAME	NUMBER	PERCENTAGE (%)
Ritalin® 10 mg tablets	480	39.97
Ritalin LA® 20 mg capsules	465	38.72
Ritalin LA® 30 mg capsules	99	8.24
Ritalin LA® 40 mg capsules	23	1.91
Ritalin SR® 20 mg tablets	134	11.16
TOTAL	**1 201**	**100.00**

Table IV illustrates the prescribing frequency of the different methylphenidate dosage forms according to patient age.

Table IV: Prescribing frequency of different methylphenidate dosage forms according to patient age

AGE (in years)	Ritalin®	Ritalin LA®	Ritalin SR®	TOTAL	PERCENTAGE (%)
1	0	2	0	2	0.17
2	1	0	0	1	0.08
3	3	2	0	5	0.42
5	3	0	0	3	0.25
6	17	2	1	20	1.67
7	45	12	2	59	4.91
8	89	52	9	150	12.49
9	78	73	10	161	13.41
10	82	99	16	197	16.40
11	44	94	19	157	13.07
12	33	85	20	138	11.49
13	32	57	20	109	9.08
14	19	33	14	66	5.50
15	11	30	13	54	4.50
16	6	16	6	28	2.33
17	11	16	3	30	2.50
18	6	14	1	21	1.75
TOTAL	**480**	**587**	**134**	**1 201**	**100.00**

More than 80% of methylphenidate prescriptions were for quantities of 30 or 60 tablets or capsules (see Table V). Only 28.56% of methylphenidate prescriptions were, however, classified as chronic prescriptions.

Table V: Quantities dispensed per dosage form of methylphenidate

QUANTITY (in tablets or capsules)	DOSAGE FORMS			TOTAL	
	CAPSULES	SUSTAINED-RELEASE TABLETS	TABLETS	NUMBER	%
Less than 30	41	15	47	103	8.57
30	469	98	348	915	76.19
31–59	22	5	31	58	4.83
60	41	15	35	91	7.58
More than 60	14	1	19	34	2.83
TOTAL	**587**	**134**	**480**	**1 201**	**100.00**

As can be seen in Table VI, most methylphenidate prescriptions were for MR capsules (48.87%), followed by 10 mg tablets (39.97%) and sustained-release tablets (11.16%). Acute prescriptions are generally once-off prescriptions for a condition normally of an acute nature. It is also possible that a prescription is claimed as an acute prescription while awaiting approval (pre-certification) from the medical aid scheme to receive the medicine on a chronic basis. A chronic prescription is generally defined as a prescription for a period of at least three months for a potentially life-threatening condition that requires longer-term treatment. The terms "acute" and "chronic" were allocated by the medical aid administrator to the different prescriptions according to their standard classification system that they use for all the medical aid schemes that they administer. Prescribing differences were observed between the different trade names for acute and chronic prescriptions ($\chi 2 = 6.23$; d.f. = 2; $p \leq 0.05$). There were more chronic prescriptions for Ritalin LA® capsules and more acute prescriptions for Ritalin® tablets.

Table VI: Acute and chronic methylphenidate prescriptions according to trade name

TRADE NAME	PERCENTAGE (%)*		TOTAL	
	ACUTE (n = 858)	CHRONIC (n = 343)	NUMBER	%
Ritalin®	42.19	34.40	480	39.97
Ritalin LA®	46.97	53.65	587	48.87
Ritalin SR®	10.84	11.95	134	11.16
TOTAL	**100.00**	**100.00**	**1 201**	**100.00**

* $\chi 2 = 6.23$; d.f. = 2; $p \leq 0.05$.

Methylphenidate prescribing in the different provinces

Methylphenidate represented 1.81% (1 201 of 66 450 prescription items) of all prescriptions to children and adolescents, with the highest average percentages in the Western Cape (2.58%) followed by KwaZulu-Natal (2.10%), and the lowest average percentages in the Northern Cape (0.63%) and Free State (1.16%). The percentage prescribing frequency of methylphenidate in the nine provinces is illustrated in Table VII.

From a more detailed analysis according to different areas (cities and towns in the provinces), it was evident that most prescriptions for methylphenidate were dispensed in cities (especially Johannesburg and Pretoria in Gauteng and Bellville in the Western Cape), as is illustrated in Table VIII. This is true if only prescription frequencies are considered. This was, however, not necessarily true when the number of patients

Table VII: Percentage prescribing frequency of methylphenidate in the nine provinces

PROVINCE	PERCENTAGE (%)
Eastern Cape	1.98
Free State	1.16
Gauteng	1.67
KwaZulu-Natal	2.10
Mpumalanga	1.66
North-West Province	1.38
Northern Cape	0.63
Northern Province	1.22
Western Cape	2.58
ALL PROVINCES	**1.81**

in each area was used as a denominator (as can be seen from the last column of Table VIII).

The percentage prescribing frequency and cost of methylphenidate is compared for the different provinces in Figure 1. The number of patients in each province aged 18 years and younger was as follows: Eastern Cape (2 232 patients), Free State (1 301 patients), Gauteng (16 989 patients), KwaZulu-Natal (5 075 patients), Mpumalanga (1 723 patients), North-West Province (1 489 patients), Northern Cape (341 patients), Northern Province (664 patients) and Western Cape (4 919 patients), giving a total of 34 733 patients in the nine provinces.

The prescribing frequency of methylphenidate dosage types in the different provinces is illustrated in Figure 2. The average age of patients receiving methylphenidate was 10.87 (SD = 2.79; median = 10.51) years. The average age of patients receiving Ritalin® was 9.97 (SD = 2.78) years, Ritalin LA® 11.38 (SD = 2.66) years and Ritalin SR® 11.97 (SD = 2.46) years. The immediate release products were therefore given, in general, to younger patients.

Figure 1: Percentage prescription frequency and cost of methylphenidate prescriptions in the nine provinces

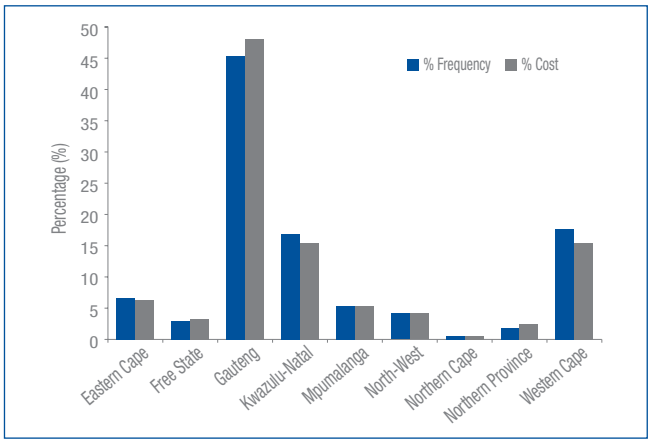


Figure 2: Distribution of methylphenidate dosage types according to provinces

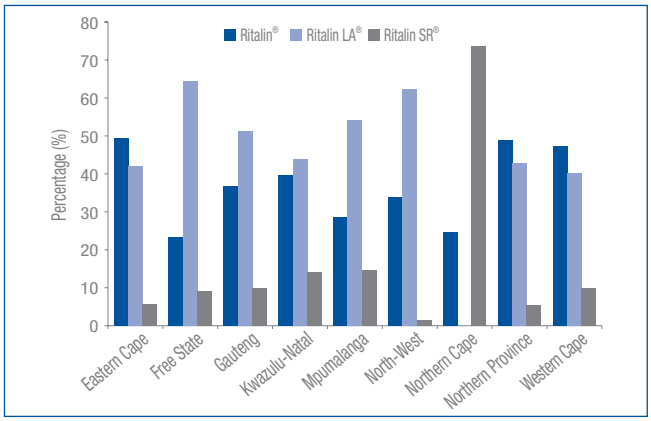


Table VIII: Areas with the most methylphenidate prescriptions

RANK	AREA	PERCENTAGE (%)		TOTAL		ALL PRODUCTS	
		ACUTE (n = 858)	CHRONIC (n = 343)	NUMBER (n = 1 201)	%	NUMBER (n = 66 405)	%
1	Pretoria	10.02	12.54	129	10.74	7 646	1.69
2	Johannesburg North	10.61	9.33	123	10.24	5 270	2.33
3	Bellville	7.34	9.91	97	8.08	2 749	3.53
4	Johannesburg	4.78	7.58	67	5.58	4 161	1.61
5	Johannesburg Central Business District (CBD)	5.01	3.21	54	4.50	3 295	1.64
6	Durban	3.96	4.08	48	4.00	2 048	2.95
7	Port Elizabeth	4.43	2.92	48	4.00	1 628	2.95
8	Edenvale	4.20	2.33	44	3.66	2 413	1.82
9	Pietermaritzburg	2.68	5.54	42	3.50	1 109	3.79
10	Cape Town	3.15	3.79	40	3.33	2 025	1.98
11	Alberton	2.45	2.33	29	2.41	1 546	1.88
12	Kempton Park	2.45	2.04	28	2.33	1 946	1.44
13	Klerksdorp	1.98	1.75	23	1.92	972	2.37
14	Nelspruit	2.33	0.87	23	1.92	752	3.06
15	Stellenbosch	1.63	2.04	21	1.75	668	3.14
16	Benoni	1.40	2.33	20	1.67	1 266	1.58
17	Pinetown	1.17	2.92	20	1.67	804	2.49
18	Bloemfontein	1.98	0.58	19	1.58	1 308	1.45
19	East London	1.86	0.58	18	1.50	848	2.12
20	Bluff	1.75	0.29	16	1.33	507	3.16

Dosages of methylphenidate prescribed

The Defined Daily Dose (DDD) for methylphenidate is 30 mg (oral).[14] The DDD corresponds to what is assumed to be the average dose per day for a drug, when it is used in its main indication in adults.[17] No DDD has been established for use in children, and since the focus of this study was on patients aged 18 years and younger, the average Prescribed Daily Dose (PDD) cannot be directly compared to the DDD. The DDD, however, remains a useful measurement unit for comparative purposes.

The average PDD for methylphenidate prescriptions in this study was 19.27 (SD = 11.87) mg, as can be seen in Table IX. The average PDD for acute methylphenidate prescriptions was 18.48 (SD = 11.02) mg, and for chronic prescriptions 21.25 (SD = 13.60) mg. In this study, 20 mg was the most popular PDD (42.63% of prescriptions), followed by 10 mg (30.22% of prescriptions). This finding is different from a previous South African study[18] where it was found that 10 mg was the most popular PDD (40.9% of prescriptions), followed by 20 mg (33.0% of prescriptions).

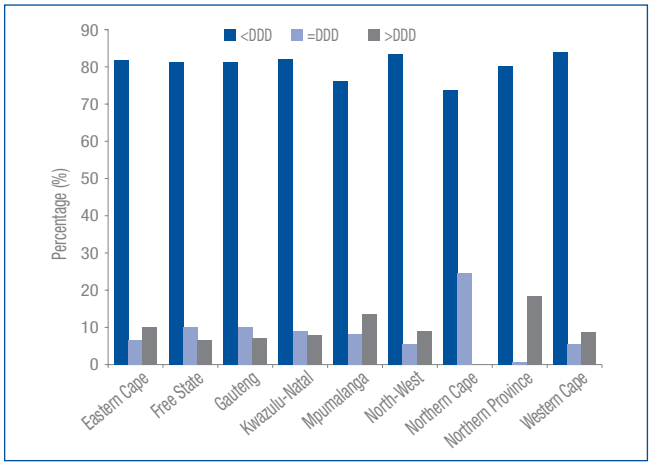
On average, only 8.74% of prescriptions for methylphenidate were prescribed in the DDD of 30 mg. Most of the prescriptions (82.93%) were in doses lower than the DDD. This pattern was

Table IX: Average PDDs for chronic and acute methylphenidate prescriptions per province

PROVINCE	AVERAGE AGE (in years)	AVERAGE PDD (in mg)		
		ACUTE	CHRONIC	TOTAL
Eastern Cape	10.57	16.83	21.67	17.77
Free State	11.29	20.24	26.53	21.45
Gauteng	10.68	18.41	21.00	19.15
KwaZulu-Natal	11.51	17.03	23.23	19.01
Mpumalanga	10.88	19.45	22.08	20.08
North-West Province	10.18	19.13	22.14	20.27
Northern Cape	9.23	23.33	-	23.33
Northern Province	11.21	20.42	13.33	19.00
Western Cape	10.98	19.80	19.27	19.64
ALL PROVINCES	**10.87**	**18.48**	**21.25**	**19.27**

consistent for all nine provinces (see Figure 3). This was to be expected, since the dose for children and adolescents should be lower than the adult dose (the DDD). This finding confirms that in clinical practice, methylphenidate dosages are related to body weight and age of the patient, and that a standard dose for all patients is not appropriate.

Figure 3: PDDs of methylphenidate in relation to the DDD according to provinces



Conclusion and recommendations

ADHD has an impact on an individual's psychological development, education and relationships, and also affects the family. It has been increasingly shown that ADHD often continues into adolescence and adulthood. These are aspects that warrant further research and could not be investigated in this study due to the limitations of prescription database studies.

Methylphenidate remains the mainstay in the treatment of ADHD. This study investigated methylphenidate prescribing and the population receiving these prescriptions. The results of this study were generally in agreement with those of previous South African studies. It was found that most methylphenidate prescriptions (63.14%) were issued to children between seven and twelve years of age, most prescriptions were for 30 tablets or capsules, and the average PDD for methylphenidate was 19.27 mg. Numerous claims are being made that methylphenidate is overused or even abused, especially in children of school-going age. Most prescriptions, based on frequency, were issued in metropolitan areas (cities) in this study, but overuse could not be established.

Not many studies have been published that investigate drug utilisation or prescribing differences between the nine provinces in South Africa and no similar study could be found for methylphenidate. This study has limitations, in that it was a cross-sectional study, the study only covered a small percentage of the private health care sector in South Africa and the recent introduction of more and newer products for ADHD were not covered in this study. This study must therefore be seen as a preliminary study to provide some baseline information of methylphenidate prescribing for ADHD in the different provinces of South Africa that can lead to more comprehensive studies in future.

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