# Self-reported use of methylphenidate by hostel students at a South African tertiary academic institution

**J Dreyer**

**22155252**

Dissertation submitted in partial fulfilment of the requirements for the degree Magister Pharmaciae in Pharmacy Practice at the Potchefstroom Campus of the North-West University

Supervisor: Dr JR Burger

Co-supervisor: Mrs I Kotze

Co-supervisor: Prof S van Dyk

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# PREFACE

The following dissertation was written in article format. As specified by the requirements of the North-West University, the chapter containing the results (Chapter 3) is presented in the form of manuscripts and any results not discussed in the manuscripts are discussed separately at the end of Chapter 3. The two manuscripts have been submitted for publication to the journals *Health SA Gesondheid* and the *South African Medical Journal* (proof of submission is given in Annexures B and C). Each of the manuscripts has been written in accordance to the author guidelines specified by the respective journals (refer to Annexures D and E). The manuscripts have their own separate reference lists written as required by the journal. In addition the references cited in the manuscripts and throughout the dissertation are listed according to the referencing style of the North-West University in the complete reference list at the end of the dissertation.

The dissertation is divided into four chapters. Chapter 1 gives an overview of the study, the problem statement, research objectives and a description of the method of investigation. Chapter 2 is a comprehensive literature review to fulfil the literature objectives of the study. Chapter 3 contains the manuscripts and additional results. The final chapter is comprised of conclusions, recommendations and study limitations and strengths. The annexures and complete reference list follow at the end.

# ACKNOWLEDGEMENTS

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# ABSTRACT

**Key terms:** methylphenidate, nonmedical use, illicit use, misuse, abuse, diversion, reasons for use, off-label use, side effect, adverse effect, extended release, immediate release.

The study set out to determine the extent and nature of methylphenidate use by hostel students from a South African tertiary academic institution. The study was executed in two phases: the literature phase and empirical phase. The literature phase involved a comprehensive literature review that served the purpose of contextualising the study. The empirical phase entailed a quantitative cross-sectional study that used a structured questionnaire to obtain data. The study population consisted of 328 voluntary participants from ten randomly selected hostels at a South African tertiary academic institution.

Data were captured using Excel® and analysed using IBS SPSS Statistics 22. Descriptive statistics included frequencies, means, standard deviations and percentages. Categorical data were analysed with the Chi-square ($\chi^2$) test and tested for significance using Pearson's correlation coefficient. Effect sizes were determined with Cramer's *V* where ~0.1 was indicative of a small effect, ~0.3 of a medium effect and 0.5 or larger of a large effect. Numerical data were analysed using a student *t*-test. A result was considered to be statistically significant when $p \leq 0.05$.

The results revealed that one in four hostel students have used methylphenidate at least once in their lives. Half of the students who have had prescribed methylphenidate prescribed to them have never been diagnosed with ADHD. The majority of all users have used methylphenidate during their time at university (79.8%) and most of the methylphenidate users started using the drug in high school or university (89.6%). Medical users were more likely to use methylphenidate every day (45.8% *vs.* 11.3%; $p=0.001$) while nonmedical users tended to rely on methylphenidate before examinations (73.6%) and semester tests (43.4%). The most common reasons for methylphenidate use were for academic purposes. Recreational reasons for use were uncommon. No correlation could be found between methylphenidate use and demographic characteristics.

Approximately 86% of all users have experienced adverse effects due to methylphenidate use, the most common of which were sleep difficulties and reduced appetite. Students more often reported they have used extended release methylphenidate (85.7%) than immediate release (14.3%). Unfortunately, due to low reported rates, no analysis could be conducted for the route of administration used. Both medical and nonmedical users have used illicit sources to acquire methylphenidate, for instance 58.8% of all users have acquired it from friends. Finally, users were found to be more knowledgeable about methylphenidate than non-users ($p=0.002$).

The study shows that hostel students from a South African tertiary academic institution divert methylphenidate and use it in nonmedical ways. It also provides evidence to suggest that a large proportion of methylphenidate prescriptions are not for the two registered uses.

# OPSOMMING

**Trefwoorde:** metielfenidaat, niemediese gebruik, onwettige gebruik, misbruik, afwending, redes vir gebruik, niegoedgekeurde gebruik, newe-effek, nadelige uitwerking, verlengde vrystelling, onmiddelike vrystelling.

Hierdie studie het ten doel gehad om die omvang en aard van metielfenidaatgebruik onder koshuisstudente by ’n Suid-Afrikaanse tertiêre instelling te bepaal. Die studie het twee fases behels: ’n literatuurstudie en ’n empiriese ondersoek. Die literatuurstudie was in die vorm van ’n omvattende literatuuroorsig om die studie te kontekstualiseer. Die empiriese fase het ’n kwantitatiewe deursneestudie behels met data wat deur ‘n gestruktureerde vraelys ingewin is. Die studiepopulasie was 328 vrywillige deelnemers van tien ewekansig geselekteerde koshuise by ’n Suid-Afrikaanse tertiêre akademiese instelling.

Data is met Excel® vasgelê en met IBS SPSS Statistics 22 ontleed. Beskrywende statistiek het frekwensies, gemiddelde, standaardafwykings en persentasies ingesluit. Kategoriese data is deur die chi-kwaaddraadtoets ($\chi^2$) ontleed en vir statistiese betekenis getoets met Pearson se korrelasiekoëffisiënt. Effekgrootte is deur Cramer se $V$ bepaal waar ~0.1 ’n klein effek, ~0.3 ’n medium effek en 0.5 of meer ’n groot effek aandui. Numeriese data is deur ’n studente $t$-toets ontleed. ’n Resultaat is as statisties betekenisvol beskou as $p \leq 0.05$.

Die resultate het bewys dat een in vier van die koshuisstudente ten minste een keer in hulle lewens metielfenidaat gebruik het. Die helfte van die studente vir wie metielfenidaat voorgeskryf is, is nooit met aandagafleibaarheidhiperaktiwiteitsindroom gediagnoseer nie. Die meerderheid van al die gebruikers het metielfenidaat gedurende hulle tyd op universiteit gebruik (79.8%) en die meeste van die metielfenidaatgebruikers het die middel tydens hoërskool of universiteit begin gebruik (89.6%). Mediese gebruikers was meer geneig om metielfenidaat elke dag te gebruik (45.8% teenoor 11.3%; $p$=0.001) terwyl niemediese gebruikers geneig was om op metielfenidaat staat te maak voor eksamens (73.6%) en semestertoetse (43.4%). Die mees algemene gebruike for metielfenidaatgebruik was om akademiese redes. Gebruik vir ontspanning was raar. Geen korrelasie kon tussen metielfenidaatgebruik en demografiese eienskappe bepaal word nie.

Ongeveer 86% van al die gebruikers het nadelige uitwerkings as gevolg van metielfenidaatgebruik ondervind. Die meese algemene nadelige uitwerkings was slaaprobleme en afname in aptyt. Studente het aangedui dat hulle meer dikwels metielfenidaat in verlengde vrystellingsvorm (85.7%) as onmiddelike vrystellingsvorm (14.3%) gebruik. Ongelukkig kon geen ontleding van die metode van toediening geskied nie as gevolg van die lae rapporteringskoers. Van die mediese sowel as die niemediese gebruikers het al onwettige

bronne gebruik om metielfenidaat te bekom, byvoorbeeld 58.8% van alle gebruikers het dit van vriende verkry. Laastens is bevind dat gebruikers meer kennis oor metielfenidaat gedra het as niegebruikers ($p$=0.002).

Die studie toon dat koshuisstudente van ’n Suid-Afrikaanse tertiëre akademiese instelling metilfenidaat afwend en dit op niemediese wyses gebruik. Dit lewer ook bewyse wat voorstel dat ’n groot proporsie van metielfenidaatvoorskrifte nie vir die twee geregistreerde gebruike uitgereik word nie.

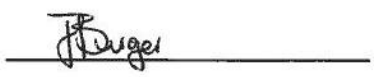
## AUTHORS' CONTRIBUTIONS TO MANUSCRIPT 1

The contributions of each of the authors of manuscript 1, "Appropriate and non-medical use of methylphenidate by South African university residence students: prevalence, reasons for use and adverse effects", were as follows:

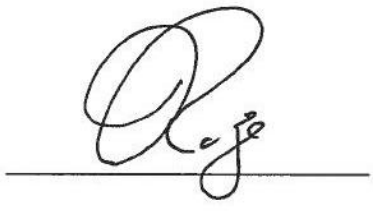
| Author | Role in study |
|---|---|
| Ms J Dreyer | Planning and designing the study<br>Conducting the literature review<br>Collecting and capturing the data<br>Interpreting the results<br>Writing the manuscript |
| Dr JR Burger<br>(Supervisor) | Supervising the study conceptualisation and design<br>Guiding the interpretation of the results<br>Revising the manuscript |
| Mrs I Kotze<br>(Co-supervisor) | Co-supervising the study conceptualisation and design<br>Revising the manuscript |
| Prof S van Dyk<br>(Co-supervisor) | Co-supervising the study conceptualisation and design<br>Revising the manuscript |
| Mrs M Cockeran | Guiding the study conceptualisation and design<br>Analysing the data<br>Verifying the results from the statistical analysis |

With the following statement the co-authors confirm their role in the study and give their permission that the manuscript may form part of this dissertation.

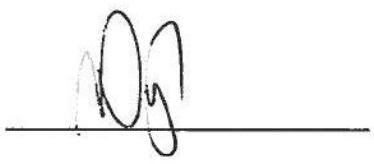
*I declare that I have approved the above mentioned manuscript and that my role in this study, as indicated above, is representative of my actual contributions and I hereby give my consent that it may be published as part of the MPharm study of J Dreyer.*



Dr JR Burger



Mrs I Kotze



Prof S van Dyk

Mrs M Cockeran

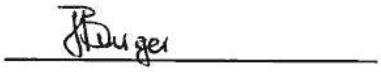
## AUTHORS' CONTRIBUTIONS TO MANUSCRIPT 2

The respective contributions of the authors of the second manuscript, "Diversion and perceived availability of methylphenidate in a South African tertiary academic institution", were:

| Author | Role in study |
|---|---|
| Ms J Dreyer | Planning and designing the study<br>Conducting the literature review<br>Collecting and capturing the data<br>Interpreting the results<br>Writing the manuscript |
| Dr JR Burger<br>(Supervisor) | Supervising the study conceptualisation and design<br>Guiding the interpretation of the results<br>Revising the manuscript |
| Mrs I Kotze<br>(Co-supervisor) | Co-supervising the study conceptualisation and design<br>Revising the manuscript |
| Prof S van Dyk<br>(Co-supervisor) | Co-supervising the study conceptualisation and design<br>Revising the manuscript |
| Mrs M Cockeran | Guiding the study conceptualisation and design<br>Analysing the data<br>Verifying the results from the statistical analysis |

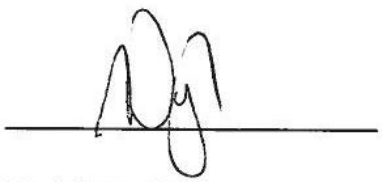
With the following statement the co-authors confirm their role in the study and give their permission that the manuscript may form part of this dissertation.

*I declare that I have approved the above mentioned manuscript and that my role in this study, as indicated above, is representative of my actual contributions and I hereby give my consent that it may be published as part of the MPharm study of J Dreyer.*

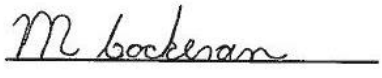


Dr JR Burger

Mrs I Kotze



Prof S van Dyk



Mrs M Cockeran

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# LIST OF ACRONYMS AND ABBREVIATIONS

AACAP = American Academy of Child and Adolescent Psychiatry

ADHD = Attention-deficit/hyperactivity disorder

ANOVA = Analysis of variance

ASRS = Adult ADHD self-report scale

BEACH-Q = Behaviours, expectancies, attitudes and college health questionnaire

BMI = Body mass index

CASA = National Centre on Addiction and Substance Abuse

CES1 = Carboxylesterase 1

CNS = Central nervous system

D1 = Dopamine receptor 1

D2 = Dopamine receptor 2

DA = Dopamine

DAT = Dopamine transporter

DAWN = Drug Abuse Warning Network

DDD = Defined daily dose

DUI = Driving under the influence

DWI = Driving while intoxicated

E = Expected value

FDA = Food and Drug Administration (United States of America)

GHB = Gamma hydroxybutyrate

HIV = Human immunodeficiency virus

HMO = Health maintenance organisation

HREC = Health Research Ethics Committee, Faculty of Health Sciences, North-West University

INCB = International Narcotics Control Board

LSD = Lysergic acid diethylamide

MCC = Medicine Control Council

MDMA = 3,4-methylenedioxymethamphetamine

MPH = Methylphenidate

NE = Norepinephrine

NET = Norepinephrine transporter

NSDUH = National Survey on Drug Use and Health

NMDA = N-methyl-D-aspartate

O = Observed value

OROS = Osmotic release oral system

RCT = Randomised controlled trial

SAMHSA = Substance Abuse and Mental Health Services Administration (United States of America)

SAPC = South African Pharmacy Council

THC = delta-9-tetrahydocannibinol

UK = United Kingdom

USA = United States of America

WHO = World Health Organization

$\chi^2$ = Chi-square

# GLOSSARY

For the purpose of this research project, these concepts were defined as follows:

- Authorised prescriber: According to the Medicines and Related Substances Control Act (Act 101, 1965), an authorised prescriber is “a medical practitioner, dentist, veterinarian, practitioner, nurse or other person registered under the Health Professions Act, 1974”.
- Medical use of methylphenidate: The appropriate use of the drug, as prescribed by an authorised prescriber, by the person to whom it was prescribed.
- Nonmedical use of methylphenidate: The incorrect use of methylphenidate (e.g. for inappropriate reasons and/or excessively) and/or the use of methylphenidate for any reason by a person to whom the drug was not prescribed.
- Diversion: The illegal deviation of regulated pharmaceuticals from legal sources to the illicit marketplace (Smith *et al.,* 2013:2292), for example, giving or selling prescription medication to someone who does not have a prescription for it.

# CHAPTER 1: INTRODUCTION AND SCOPE OF THE STUDY

## 1.1 Background

The effect of stimulants on behaviour was first discovered by Charles Bradley in 1937. His discoveries ultimately led to studies of the stimulant methylphenidate for use in attention-deficit/hyperactivity disorder (ADHD) (Strohl, 2011:27), which is one of the most common drugs prescribed for this condition in modern times (AACAP, 2002:26S). Methylphenidate has, *inter alia,* also been used off-label for the treatment of amphetamine dependence; anaesthesia recovery; apathy in Alzheimer's disease; brain trauma; cocaine dependence; delirium; dementia; depression; familial male precocious puberty; fatigue in cancer, multiple sclerosis and human immunodeficiency virus (HIV) infection; obesity; giggle incontinence; Parkinson's disease; and weaning from mechanical ventilation (refer to Table 2-1).

The use of prescription stimulants such as methylphenidate on college campuses has been documented in Australia, Europe (Belgium, France, Germany, Ireland, Italy, Netherlands, Switzerland and the United Kingdom), North America (Canada and the United States of America), South America (Brazil), as well as the Middle East (Iran) (Barrett *et al.,* 2005:458; Table 5-1). According to Herman-Stahl *et al.* (2007:1011) and Johnston *et al.* (2013:26,344), college students in their studies were more at risk of using prescription stimulants for nonmedical reasons than young adults who are not enrolled in a college. Studies have also suggested that students in hostels (sororities or fraternities) are at even greater risk for nonmedical stimulant use (Bavarian, Flay & Smit, 2014:141; DeSantis *et al.,* 2008:317; McCabe, 2008b:717; McCabe *et al.,* 2005:99; Shillington *et al.,* 2006:1006; Weyandt *et al.,* 2009:293). In general, the prevalence of lifetime nonmedical prescription stimulant use among college students was estimated to be between 0.8% and 37.4% (Table 5-1). In the study conducted by Teter *et al.* (2003:614), students who used prescription stimulants also used more alcohol and illicit drugs than students who did not report any stimulant use. In addition, McCabe and Teter (2007:69) concluded that nonmedical users of prescription stimulants were more likely to engage in poly-drug use. The authors suggested that nonmedical users, especially those who use these stimulants via non-oral administration routes, should be screened for potential drug abuse. In other words, the nonmedical use of prescription stimulants should not be seen as an isolated behaviour to gain a competitive edge, but rather as part of the larger problem of potentially dangerous behaviour (Arria & DuPont, 2010:425).

One of the prescription stimulants used by college students for nonmedical reasons is methylphenidate (Teter *et al.,* 2003:614). One of the first records of methylphenidate abuse dates back to 1960 (Rioux, 1960:348). Ritalin® has allegedly been used for study purposes in South Africa (Swanepoel, 2012; Hunter, 2014; Meyer, 2015; Venter, 2014; Cilliers, 2015). There have also been reports of South African students snorting methylphenidate (Green, 2013). There is, however, a lack of general information regarding the prevalence of methylphenidate use among university students in South Africa.

In a systematic review conducted by Finger *et al.* (2013:287), the following reasons for illicit methylphenidate use were identified: recreational, to stay awake, weight loss[1], improvement of cognitive performance, improvement of academic achievement, curiosity, improvement of self-confidence and environmental pressure. Mazanov *et al.* (2013:113) found that students generally use prescription stimulants for an effect (such as improved concentration) and not an outcome (for example, to get a better job). The illicit use of methylphenidate has several considerations, which include the insufficient control of the drug (Arria & DuPont, 2010:419) and the potential harm that may result from nonmedical use (White *et al.,* 2006:266).

In terms of legally required control, methylphenidate is classified as a schedule 6 substance in South Africa (Rossiter, 2014:508). The Medicines and Related Substances Control Act (Act 101, 1965) states that schedule 6 medicines may not be used for any reason besides medical purposes unless one is authorised to do so by the Minister of Health. Furthermore, there are restrictions on who may sell and import schedule 6 medicines. Lastly, the Act states that the volume of a schedule 6 substance that may be dispensed at one time is limited to the quantity needed for 30 days. The availability of methylphenidate for illicit use is therefore concerning (Arria & DuPont 2010:419) as it indicates a potential inadequacy in the medicine's control. According to Adams and Kopstein (1993:116), this inadequacy forms part of the problem with drug abuse. The main source of methylphenidate was found to be students' peers (Bavarian, 2012:102; DeSantis *et al.,* 2008:320). DeSantis *et al.* (2008:320) indicated that 89% of the students in their study (N=1811) who used ADHD medication illicitly obtained the medication from their peers. Rabiner *et al.* (2009a:151) concluded that in the six months preceding their study, 56% of the students (N=115) who had a prescription for methylphenidate were approached and asked to divert their medication. Twenty-five present of those students had done so.

[1] Weight loss is an off-label use of methylphenidate; however, the use thereof was determined to be illicit in this review since these users did not have prescriptions for the drug (Finger *et al.,* 2013:287).

In terms of the potential harm to students who misuse methylphenidate, White *et al.* (2006:226) found that students who abuse methylphenidate may be unaware or unconcerned of the harm methylphenidate may cause them. Common adverse effects of methylphenidate include headaches, dizziness, tachycardia, palpitations, arrhythmia, changes in blood pressure, dyskinesia, nervousness, insomnia, irritability, nausea, abdominal pain and loss of appetite (Klein-Schwartz, 2002:220; Rossiter, 2014:508). Other side effects are anger and fear (Loughlin & Generali, 2006:891). A study conducted by Rabiner and colleagues (2009a:150) confirmed that the most common side effects that students experience are decreased appetite (74%), insomnia (63%), irritability (52%) and headaches (51%). In 2007, the Food and Drug Administration warned that methylphenidate may cause sudden death due to serious adverse cardiovascular effects (FDA, 2007). Even though methylphenidate overdoses usually result in a moderately severe clinical presentation, fatalities have occurred (Spiller *et al.,* 2013:535). Furthermore, students may become addicted to the increased energy and sense of well-being generated by methylphenidate use (National Institute on Drug Abuse, 2001).

Besides the drug's inert risk, the way in which students use methylphenidate is also potentially dangerous (Teter *et al.,* 2006:1508). The most common route of administration is orally; however, students also administer the drug via the intranasal and intravenous routes (DuPont *et al.,* 2008:169; Finger *et al.,* 2013:287). Teter *et al.* (2010:295) found higher rates of depressed moods in students who use prescription stimulants by non-oral routes. As early as the 1990s and early 1970s, deaths have occurred from both intranasal (Massello & Carpenter, 1999:220) and intravenous use (Lewman, 1972:68; Parran & Jasinski, 1991:781; Stern *et al.,* 1994:559).

The concomitant use of other substances, such as alcohol and marijuana, with prescription stimulants is common (Novak *et al.,* 2007; Rabiner *et al.,* 2009a:150). In 2004, there were 8 000 cases of emergency room admissions in the United States of America due to ADHD medications, with 48% of those cases being nonmedical users. Of the nonmedical users, 68% had used the ADHD medications with alcohol or other substances (DAWN, 2006:2). A study by Rabiner and colleagues (2009a:150) showed that 30% of the students with a prescription for ADHD medication (N=115) had used their medication with alcohol and 16% had used it with marijuana in the six months preceding the study. In another study at eight universities, 46.4% of the students who used prescription stimulants for nonmedical reasons in the preceding year had used it with alcohol (Egan *et al.,* 2013:75). In this regard, few students were concerned about the potential drug interactions (Low & Gendaszek, 2002:287). Little is known about the consequences of concurrent alcohol use with prescription stimulants (Egan *et al.,* 2013:75); however, deaths have been reported (Markowitz *et al.,* 1999:363). Besides concern for pharmacological interactions, students who use alcohol and prescription stimulants

simultaneously are at greater risk for substance abuse and adverse consequences (Egan *et al.,* 2013:75).

## 1.2 Problem statement

There is evidence that methylphenidate is used on university campuses in illegal ways. This illegal use includes the use of methylphenidate, for any reason, without a prescription, as well as the incorrect use of methylphenidate despite having a prescription for it. This type of use has both legal and health implications for students. Substantial research has been conducted in the United States of America (USA) and other countries, showing prevalence rates of nonmedical use between 2% and 23%, as displayed in Table 5-1. Anecdotal evidence suggests that the same problem may be present at South African universities, yet the extent thereof is unknown. This study aimed to fill this gap by providing answers to the following research questions:

- What is methylphenidate and what are its indications?
- How do students use methylphenidate?
- What is the prevalence of the use of methylphenidate among hostel students at universities?
- What are the reasons for the use of methylphenidate by hostel students?
- What do students know about the use of methylphenidate?
- How do students acquire methylphenidate?
- What are the side effects experienced because of methylphenidate use?
- What are the legal aspects of diversion and methylphenidate use?

## 1.3 Study aim and objectives

### 1.3.1 General aim

The aim of the study was to determine the self-reported use of methylphenidate by hostel students at a South African tertiary academic institution.

### 1.3.2 Study objectives

The study was carried out in two phases, namely the literature and empirical phases. Therefore, the study had both literature objectives and empirical objectives.

#### 1.3.2.1 Literature objectives

The literature objectives were to:

(1) describe methylphenidate as a pharmacological entity with regard to its mechanism of action, adverse effects and drug interactions;
(2) describe the registered and off-label indications for the use of methylphenidate;
(3) determine the national and international prevalence and epidemiology of the use of methylphenidate, for medical and nonmedical reasons; and
(4) describe the legal aspects of methylphenidate diversion and use.

#### 1.3.2.2 Empirical objectives

The second phase of the study was conducted at a South African tertiary academic institution. The empirical objectives and sub-objectives were to:

(1) determine how many hostel students use methylphenidate;
(a) determine the lifetime prevalence[2] of methylphenidate use by all the students and the user subgroups (refer to Figure 1-1);
(b) determine the prevalence of methylphenidate use during the students' time at university in the subgroups displayed in Figure 1-1;
(2) determine the relationship between demographic information and the use of methylphenidate;
(3) determine the relationship between the manner of methylphenidate use and the formulation of methylphenidate products;
(a) determine the difference in formulations used by the different types of users;
(b) determine the average doses used for each product;
(c) clarify the relationship between how methylphenidate is used in terms of the route of administration and the type of formulation used;
(4) determine the initiation to and frequency of using methylphenidate;
(a) determine when (before primary school, during primary school, during high school, during university or during another period) methylphenidate use first started in the various subgroups of methylphenidate users;
(b) determine the frequency of methylphenidate use by the different subgroups;
(5) ascertain the reasons why hostel students use methylphenidate;
(a) establish the reasons why students in the different subgroups use methylphenidate;

[2] Lifetime prevalence refers to percentage of students who have used methylphenidate at any point in time during their life (Finger *et al.,* 2013:286).

(b) confirm whether students who use methylphenidate for ADHD have ever been diagnosed with ADHD by a healthcare professional;

(6) determine the side effect profile the students experience when using the drug;

(a) determine the number of side effects that students experience in relation to the type of user;

(b) determine the types of side effects experienced in relation to the type of user;

(c) determine the correlation between the number of side effects experienced and the average dose used;

(d) establish the relationship between the route of administration and the number of side effects experienced;

(7) identify sources of diversion and perceived availability of the drug;

(a) identify the sources of methylphenidate between the different types of nonmedical users;

(b) compare the perceived available sources of methylphenidate between methylphenidate users and non-users and between the user subgroups;

(c) compare the perceived ease of acquisition of methylphenidate between students who use methylphenidate and those who do not, as well as between the various user subgroups;

(d) clarify the perceived ease of acquiring methylphenidate from prescribers between non-users of methylphenidate and the user subgroups; and

(8) ascertain the differences in the students' knowledge with regard to the use of methylphenidate between non-users of methylphenidate and the user subgroups.

Table 1-1 displays how these empirical objectives are discussed in Chapter 3.

**Table 1-1: Distribution of the empirical objectives as discussed in Chapter 3**

| Section of Chapter 3 | Specific research objectives |
|---|---|
| 3.1 Manuscript 1:<br>"Appropriate and non-medical use of methylphenidate by South African university residence students: prevalence, reasons for use and adverse effects" | (1) determine how many hostel students use methylphenidate;<br>(2) determine the relationship between demographic information and the use of methylphenidate;<br>(4) determine the initiation to and frequency of using methylphenidate;<br>(b)<br>ascertain the reasons why hostel students use methylphenidate; |
| 3.2 Manuscript 2:<br>"Diversion and perceived availability of methylphenidate in a South African tertiary academic institution" | (3) determine the relationship between the manner of methylphenidate use and the formulation of methylphenidate products;<br>(6) determine the side effect profile the students experience when using the drug;<br>(7) identify sources of diversion and perceived |

**Table 1-1: Distribution of the empirical objectives as discussed in Chapter 3**

| Section of Chapter 3 | Specific research objectives |
|---|---|
| | availability of the drug; |
| 3.3 Additional results | (8) ascertain the differences in the students' knowledge with regard to the use of methylphenidate between non-users of methylphenidate and the user subgroups. |

## 1.4 Research methodology

The study was executed in two phases, namely the literature phase and the empirical phase. The research project commenced after obtaining the relevant permission, i.e. ethical approval from the Health Research Ethics Committee of the North-West University (the HREC; ethics number NWU-00146-14-A1 refer to Annexure G), and a letter of permission to execute the study from the executive committee of the tertiary academic institution providing the data. The literature objectives were achieved with a comprehensive literature review. Empirical objectives were achieved by means of a quantitative cross-sectional study.

### 1.4.1 Literature phase

The literature phase was conducted by searching for the information related to the literature objectives in several databases, including PubMed, Scopus and ScienceDirect. An example of a phrase that was used in the search was "methylphenidate OR Ritalin OR Concerta AND student* AND (use OR abuse OR misuse OR illicit use OR nonmedical use)". In addition, other useful sources that were cited in the generated articles were also used. The literature search included published and unpublished articles as well as electronically available theses and dissertations.

### 1.4.2 Empirical phase

#### 1.4.2.1 Study design

The study was a quantitative cross-sectional study that used a structured questionnaire as the data collection tool. In a cross-sectional study, all the data are gathered at a specific point in time (Brink *et al.,* 2012:101). The study was quantitative in nature since it is focused on assessing measurable characteristics of human behaviour (Brink *et al.,* 2012:10).

#### 1.4.2.2 Setting, data source and population

The survey was conducted at a South African tertiary academic institution. In order to protect the reputation of the participating South African tertiary academic institution its name was removed from the protocol, dissertation and publications. All the data for the empirical phase were obtained from one questionnaire (see Annexure F). The reliability and validity of the questionnaire are discussed in paragraph 1.4.2.5.

The target population for the research project was hostel students from South African tertiary institutions and the study population was full-time, contact, hostel students at one tertiary academic institution in South Africa. University students were chosen as the target population since research shows that they are more at risk of nonmedical prescription stimulant use than their peers who do not attend university (Herman-Stahl *et al.,* 2007:1011; Johnston *et al.,* 2013:26,344). Furthermore, the project is focused on hostel students since research also shows that students in sororities and fraternities have higher rates of nonmedical stimulants use (Bavarian, Flay & Smit, 2014:141; DeSantis *et al.,* 2008:317; McCabe, 2008b:717; McCabe *et al.,* 2005:99; Shillington *et al.,* 2006:1006; Weyandt *et al.,* 2009:293).

Large hostels were targeted to ensure a good sample size. The types of students in large hostels are comparable to those in smaller hostels; therefore, this recruitment strategy does not discriminate against either group of students and was unlikely to distort the results. To make sure the recruitment is fair participants were not excluded based on gender, or race. Students who were not affiliated with sororities or fraternities were likely to have different nonmedical stimulant use profiles and therefore fall outside of the scope of this research project.

#### 1.4.2.3 Sampling

##### 1.4.2.3.1 Sampling method

The study made use of cluster random sampling (Joubert & Katzenellenbogen, 2007:98). The names of ten hostels (five sororities and five fraternities) at the chosen South African tertiary academic institution were drawn at random from two separate bags. The sampling method also had some elements of convenience sampling, since, to ensure an adequate sample size, only hostels that had more than 200 students were included in the random selection. The questionnaires and informed consent forms were distributed to all the students from the selected hostels.

#### 1.4.2.3.2 Recruitment and obtaining the sample

After randomly drawing the names of ten hostels from a bag, participants were recruited by visiting each hostel during its weekly meeting and asking for voluntary participation. The researcher explained the study during this meeting and distributed the questionnaires and informed consent forms. Participants were free to read through the informed consent form and complete the questionnaire in their own time if they elected to participate. After the participants completed the questionnaire, they placed the questionnaire in a locked and sealed box with a narrow opening at the top of the box. The informed consent forms were submitted separately into the same box. The box was kept in the possession of the hostel matron for four days. The hostel matron was asked to remind participants to submit an informed consent form in addition to the questionnaire as far as possible. If the number of signed and co-signed informed consent forms were not correlated with the number of completed questionnaires, only the correlating number of questionnaires were going to be used, while any extra questionnaires would be discarded. Fortunately the same number of questionnaires and informed consent forms were returned, so no questionnaires were discarded. Nobody had access to the box without the presence of the hostel matron. When she was not available, the box was kept in a locked room. Following the distribution of the questionnaires on the Monday evening, the participants had until 17:00 on the Friday to submit the documents. After this deadline, the researchers collected the box.

#### 1.4.2.3.3 Inclusion criteria and exclusion criteria

The inclusion criteria were hostel students who were registered, fulltime, contact students studying at the chosen tertiary academic institution for the period February to June 2015 and who volunteered to partake in the study. The exclusion criteria were firstly students who were not affiliated with sororities or fraternities, and hostel students from small hostels (housing less than 200 students). In addition, students under the age of 18 years and those who could not understand any of the three languages in which the questionnaire, informed consent form and information leaflet were available (Afrikaans, English, and Setswana) were also excluded.

#### 1.4.2.3.4 Sample size

The cluster sample of the hostels yielded an approximate total of 2 400 potential participants. The final sample size was 328 respondents. It was not known how many students attended each of the respective hostel meetings and so it is impossible to calculate the accurate response rate. Based on the maximum number of potential participants, the response rate was 13.7%.

#### 1.4.2.4 Data collection tool

The prevalence of the medical use of methylphenidate by university students has been reported to be between 1.5% (McCabe *et al.,* 2006a:274) and 2.6% (Mazanov *et al.,* 2013:113). Nonmedical prescription stimulant use has a prevalence of between 5 and 35% (Wilens *et al.*, 2008:30). Therefore, a large sample size is required to obtain meaningful results. Subsequently, a structured questionnaire was a practical approach to collecting quantitative data from a large sample.

The only data that was collected were the opinions and experiences of the participants. The questionnaire contained questions that yielded the following information:

- Demographic information (gender, age, etc.);
- The number of students with ADHD and the proportion who use methylphenidate for registered indications and otherwise;
- The reason why students use methylphenidate;
- The students' source of the drug;
- How the students use the drug (how often, how much and the route of administration);
- What the students know about methylphenidate; and
- Which side effects of methylphenidate the students experience.

##### 1.4.2.4.1 Development of the questionnaire

The questionnaire was adapted from the validated Behaviours, Expectancies, Attitudes and College Health Questionnaire (BEACH-Q) (Bavarian, 2012:294). (See paragraph 1.4.2.5.2 for more detail regarding validity.) Academic healthcare professionals were asked whether each question tested its respective construct. If the professionals disagreed, they were asked why they disagreed and how the question could be improved.

##### 1.4.2.4.2 Administration of the questionnaire

The questionnaires with the attached informed consent form and information leaflet were administered during weekly hostel meetings during May 2015. The researcher explained the study and asked for voluntary participation. The participants completed the questionnaires where and when they felt comfortable. The participants returned the questionnaires into a box that was available at the hostel matron. After four days, the researchers collected the box from the hostel matron.

Completion of the questionnaire took approximately 20 minutes. Once the participant started the questionnaire, he/she could withdraw from the study at any point prior to the submission of the questionnaire. In addition, if the participant felt too uncomfortable to answer a particular question, they could skip it. Since the questionnaire was completely anonymous and no participant could be linked to the data he/she provided, the participant could not withdraw their information after submission of the questionnaire. At the end of the questionnaire, the participants were reminded that they cannot withdraw from the study after submitting the questionnaire.

After the data had been collected, the researcher gave feedback to the students regarding methylphenidate use, including its dangers and legal implications. In addition, the Student Dean of the chosen academic institution received feedback on the analysed results. The Student Dean could relay the results to the hostel committees. Feedback was given to any individual participant who requested it.

#### 1.4.2.5 The quality of the questionnaire

##### 1.4.2.5.1 Reliability

Reliability refers to the degree of reproducibility of the results (Neuman, 2006:188). There are four types of reliability, namely stability, representative, measurement and equivalence reliability. Stable reliability refers to reliability over time. Representative reliability is the consistency of results over different subgroups: in other words, different subgroups will have similar error rates (Neuman, 2006:189). Representative reliability cannot be evaluated in this study design. Measurement reliability can be defined as dependable measuring of the variables (Neuman, 2006:189). Lastly, equivalence reliability refers to consistent results from different measurements (Neuman, 2006:190). This form of reliability was incorporated into the questionnaire by means of multiple indicators.

Neuman (2006:190) suggests the following methods to improve reliability: (1) conceptualise constructs, (2) use precise measurement and (3) use multiple indicators. The first method refers to measuring only one concept per measure. The questionnaire achieved these criteria by testing only one concept per question and by using clear, unambiguous questions. Secondly, the use of precise measurement means the questions on the questionnaire acquired specific information. It has been noted that respondents reply more accurately when asked for factual information from a specific and limited time period (Sue & Ritter, 2007:41). Therefore, where appropriate, the questions asked for information from a specific time period. In addition, where there were questions requiring rating, four or five options were provided, which also improved the reliability by increasing the precision. Multiple indicators, Neuman's third suggested method

(2006:191), are separate measurements that measure the same concept. For example, in this questionnaire, there were four questions that test the students' knowledge of methylphenidate and three testing the perceived ease of acquiring methylphenidate (refer to Annexure F). Neuman (2006:191) adds that replication (i.e. using the same definitions and measurements as previous studies) can also improve reliability. The questionnaire used in this study was adapted from the BEACH-Q survey (Bavarian, 2012:295), improving the reliability and, since the BEACH-Q survey was validated, also enhancing the validity of this questionnaire.

#### 1.4.2.5.2 Validity

Validity is the degree to which the measurement instrument measures what is true in reality (Neuman, 2006:188; Sue & Ritter, 2007:184). Validity can broadly be classified into measurement validity and non-measurement validity. The former refers to how well the conceptual and operational definitions fit together. The four types of measurement validities are (1) face validity, (2) content validity, (3) criterion validity and (4) construct validity (Neuman, 2006:192; Pietersen & Maree, 2013:216).

Face validity is the degree to which an instrument appears to measure what it should measure (Pietersen & Maree, 2013:217) and content validity is the degree to which the measuring instruments measure the entire meaning of the construct (Neuman, 2006:193). These types of validity were incorporated into the questionnaire by having it evaluated by academic healthcare professionals. Criterion validity is a type of measurement validity that relies on independent verification (Neuman, 2006:193). Since this study did not aim to yield predictive results according to a specific criterion, this form of validity was irrelevant for this study. Lastly, construct validity relates to the validity of multiple indicators (Neuman, 2006:194). Good construct validity relies on good face validity (Lavrakas, 2006). Furthermore, it can be verified with evidence from several statistical analyses, for example, factor analysis, correlation coefficients and ANOVA (Brown, 2000:10).

#### 1.4.2.5.3 Measurement errors and precision

Precision can be weakened by two types of error, namely random sampling error and measurement error (Myer & Karim, 2007:157). Biemer (2010:824) mentions another source of error that can have a detrimental effect on the precision and power of a study, namely nonresponse error. In this study, sampling error was minimised by targeting a large sample. Measurement error was minimised by asking questions that refer to a specific time period and allowing participants to respond that they have no opinion on the matter, where appropriate. There is a risk of nonresponse error when questionnaires are used. However, response rates

are higher for paper-based questionnaires than for other types, such as online questionnaires (Sax *et al.,* 2003:411). Nonresponse undermines generalisability.

According to Bethlehem and Biffignandi (2012:150), the main cause of measurement error is stratification. Stratification describes the phenomenon where participants tend to answer the first more or less acceptable answer and move on. To decrease the impact of stratification, Bethlehem and Biffignandi (2012:105) suggests the following. Firstly, all the information relevant to a specific question should be visible. Therefore, this questionnaire had no options that carried over to the next page. Secondly, they warn that participants can give arbitrary answers, especially when they have to make check marks in boxes and check more than one item (Bethlehem & Biffignandi, 2012:116). The authors suggest that instead of asking the participants to check the relevant boxes, the researcher should ask the participant to reply yes or no to each of the options. This strategy was thus used in the questionnaire (refer to Annexure F).

1.4.2.5.4 Other factors influencing the quality of data

Besides validity, reliability and measurement errors, the quality of the data can also be influenced by socially desirable answers and questionnaire design (Bethlehem & Biffignandi, 2012:150).

A socially desirable answer refers to the tendency to give the socially favourable answer, especially to sensitive questions, such as illicit drug use (Bethlehem & Biffignandi, 2012:151). According to Neuman (2006:285), social desirability bias can be reduced by phrasing questions so that the socially unfavourable answer appears less disagreeable. To this end, the questionnaire was designed to ensure that the participants did not find the questionnaire offensive. In addition, the participants were allowed to complete the questionnaires where and when they felt comfortable, and they were also be assured that their answers are anonymous.

In terms of questionnaire design, two considerations are sequence and layout (Neuman, 2006:292). The sequence of the questions should be logical to minimise confusion. Moreover, the questionnaire should not start or end with threatening questions. Neuman (2006:292) holds that the questionnaire should end with a thank you note. The layout of the questionnaire should be logical, elegant and easy to follow. Finally, instructions should be written in a different format than the questions. These suggestions were also taken into account when the questionnaire was developed.

#### 1.4.2.6 Data analysis plan

The data were analysed in consultation with a statistician, according to the research objectives listed in paragraph 1.3.2.2. The statistical analysis involved descriptive and inferential statistics. In both, the following subgroups were compared to each other[3]: non-users and users, medical and nonmedical users, and nonmedical users with prescriptions and nonmedical users without prescriptions. (Refer to Figure 1-1 for a graphic representation of these subgroups.)

"MPH users" refer to those students who have used methylphenidate, while "MPH non-users" are those who have never used methylphenidate. "Medical MPH users" are the students who have only used methylphenidate as prescribed, either for their diagnosed ADHD ("ADHD+") or for other indications ("off-label users"). The nonmedical methylphenidate users are students who have used methylphenidate without a prescription ("non-prescription holders") or those who use prescribed methylphenidate inappropriately ("medical misusers"). Medical misusers are subdivided further into those who use methylphenidate excessively, those who use it for the wrong reasons and those who use it excessively and for the wrong reasons.

[3] Where the subgroups contained too few participants for statistical power, it was not analysed.

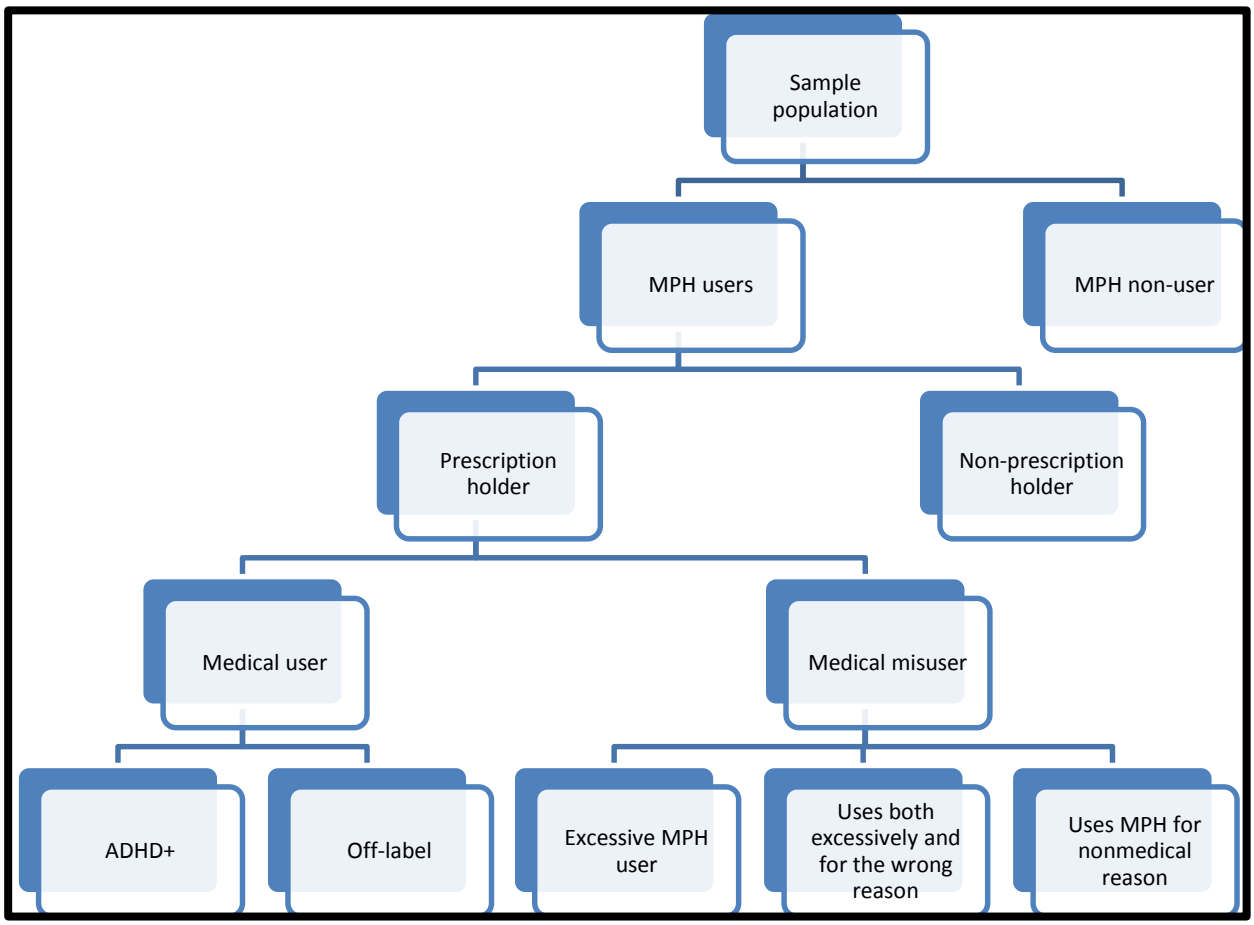


**Figure 1-1: Population distribution subgroups**

1.4.2.6.1 Descriptive statistics

Descriptive statistics were used to describe the study population and subgroups in terms of the demographic information. It was done by calculating the mean and standard deviation for continuous data, such as age, and proportions for nominal and dichotomous data, such as gender.

- Mean

The mean, also known as average, was calculated by dividing the sum of the observations by the number of observations (Pagano & Gauvreau, 2000:38).

- Standard deviation

The standard deviation[4] ($s$) is the square root of the variance, i.e. the measure of dispersion of the data (Pagano & Gauvreau, 2000:47).

$$s = \sqrt{\frac{1}{(n-1)} \sum_{i=1}^{n} (x_i - \bar{x})^2}$$

1.4.2.6.2 Inferential statistics

The inferential statistics were calculated by using the chi-square ($\chi^2$) test for categorical data and the student *t*-test for numerical data. The effect size of associations between categorical data was determined by means of Cramer's *V* statistic. A *p*-value of less than 0.05 was considered to be statistically significant.

- Chi-square ($\chi^2$) test and Cramer's *V* statistic

The chi-square test involves arranging the data in tabular format, calculating the expected value for each cell and then analysing it against the actual values per cell. In other words the observed values (O) may be represented as,

| Variable 1 | Variable 2 | | Total |
|---|---|---|---|
| | Variable 2.1 | Variable 2.2 | |
| Variable 1.1 | a | b | a+b |
| Variable 1.2 | c | d | c+d |
| Total | a+c | b+d | n |

while the expected values (E) would be

| Variable 1 | Variable 2 | | Total |
|---|---|---|---|
| | Variable 2.1 | Variable 2.2 | |
| Variable 1.1 | (a+b)(a+c)/n | (a+b)(b+d)/n | a+b |
| Variable 1.2 | (c+d)(a+c)/n | (c+d)(b+d)/n | c+d |
| Total | a+c | b+d | n |

[4] *s* = standard deviation; *n* = sample size.

The observed (O) and expected (E) values are compared using the formula[5]:

$$\chi^2 = \sum_{i=1}^{r\,c} \frac{(O_i - E_i)^2}{E_i}$$

The value obtained from this formula, together with the degrees of freedom of the table [calulated with (*r*-1)(*c*-1)], are used to look up the corresponding *p*-value (Pagano & Gauvreau, 2000:345). The strength of an association detected with the chi-square test can be measured with Cramer's *V.* Cramer's *V* is the correlation coefficient used for tables that are larger than 2x2. It is calculated as follows[6] (Rubin, 2013:213):

$$V = \sqrt{\frac{\chi^2}{N(k-1)}}$$

A Cramer's *V* result of approximately 0.1 indicates a small effect size, 0.3 indicates a medium effect size and 0.5 a large effect size (Zaiontz, 2014).

- Student *t*-test

Similarly, for the *t*-test the test statistic (*t*) is calculated and used in conjunction with the degrees of freedom ($n_1$+$n_2$-2) to look up the corresponding *p*-value by using the following formulas[7] (Pagano & Gauvreau, 2000:267):

$$S_p^2 = \frac{\sum_{i=1}^{n_1} (x_{i1} - \bar{x}_1)^2 + \sum_{j=1}^{n_2} (x_{j2} - \bar{x}_2)^2}{n_1 + n_2 - 2}$$

$$t = \frac{(\bar{x}_1 - \bar{x}_2) - (\mu_1 - \mu_2)}{\sqrt{S_p^2 \left[\left(1/n_1\right) + \left(1/n_2\right)\right]}}$$

### 1.4.3 Informed consent

Written informed consent was obtained from all participants. The participants were given information about the study (see Annexure F for the information leaflet and consent form) during a weekly hostel meeting. The information leaflet, consent form and questionnaire were available in Afrikaans, English and Setswana. Participants were made aware that refusal to participate or withdrawal would not lead to any form of reprisal. In addition, the information leaflet explained

[5] $\chi^2$ = chi-square; *r* = number of rows; *c* = number of columns; O = observed values; E= expected values
[6] Where V = Cramer's V; $\chi^2$ = chi-square; *N* = total number of cases; *k* = number of rows or columns (whichever is smaller)
[7] Where $S_p^2$ = estimated pool variance; *n* = sample size; $\bar{x}$ = sample mean; *t* = test statistic; $\mu$ = population mean

that participants may withdraw at any given time after giving informed consent until the questionnaire was submitted. The information leaflet also contained the contact details of the project leader and the HREC. Participants were free to consider their participation and sign the consent form in their own time.

## 1.5 Chapter summary

This research project aimed to investigate the medical and nonmedical use of methylphenidate by students at a South African tertiary academic institution. To that end, this Chapter 1 provided an overview, the problem statement and the method of investigation. The following chapter is a comprehensive literature review pertaining to the objectives of the literature phase of the study.

# CHAPTER 2: LITERATURE REVIEW

## 2.1 Methylphenidate

### 2.1.1 Background

Methylphenidate was synthesised by Panizzon in 1944 and marketed by the pharmaceutical company Ciba-Geigy as Ritalin® in 1954 (Morton & Stockton, 2000:159). It is a piperidine derivative with chemical structure similar to that of amphetamine (Westfall & Westfall, 2011:299). However, methylphenidate is a milder stimulant than amphetamine, has different pharmacokinetic characteristics, and has a different side-effect profile (Baumeister *et al.,* 2012:268).

In the late 1950s methylphenidate was investigated for treating in several conditions, such as depression (Robin & Wiseberg, 1958:55), recovery from thiopental-induced anaesthesia (Gale, 1958:530), and barbiturate-induced anaesthesia and poisoning (Percheson *et al.,* 1959:281). According to Baumeister and associates (2012:269) the first known suggestion to use methylphenidate for childhood behavioural disorders was made by Laufer and Denhoff in 1957. The United States Food and Drug Administration (FDA) approved methylphenidate for use in childhood behavioural disorders in 1961 (Mayes *et al.,* 2008:151), and it has remained the drug's main use for more than half a century (Volkow *et al.,* 2002:557; Wilens, 2008:S46).

### 2.1.2 Chemistry and pharmacokinetics of methylphenidate

Methylphenidate is mostly sold as a racemic mixture of two enantiomers, namely *d-threo-(R,R)*-methylphenidate and *l-threo-(S,S)*-methylphenidate. Evidence from *in vitro* systems as well as animal and clinical studies suggests that the pharmacological actions of methylphenidate can be attributed to the *d*-methylphenidate enantiomer exclusively (Ding *et al.,* 2004:174; Markowitz & Patrick, 2008:S60). Absorption after oral administration is rapid, with the plasma concentration reaching a peak in two hours. According to a review conducted by Markowitz and Patrick (2008:S56), the half-life of the *d*-enantiomer for an oral immediate release methylphenidate preparation is between 1.7 and 4.0 hours, whereas that of sustained release preparations is 2.7 to 5.3 hours. Methylphenidate is primarily eliminated by hydrolysis into ritalinic acid, a reaction that is mediated by the carboxylesterase 1 (CES1) enzyme (Sun *et al.,* 2004:474).

### 2.1.3 Mechanism of action of methylphenidate

The exact mechanism of action of methylphenidate is still somewhat elusive (Clemow & Walker, 2014:66; Epstein *et al.,* 2014:6). In a systematic review by Wilens (2008:S51), the author concluded that catecholamines play a crucial role methylphenidate's mechanism of action.

Specifically, there is evidence to suggest that methylphenidate increases extracellular concentrations of dopamine (DA), norepinephrine (NE), and possibly other neurotransmitters such as acetylcholine (Leonard *et al.,* 2004:156; Engert & Pruessner, 2008:323; Wilens, 2008:S51). In 2012, Zhang and colleagues proposed that the NMDA (N-methyl-D-aspartate) receptor may also play a role in the mechanism of action of methylphenidate. Nevels and associates (2013:29) recently summarised the mechanism of action of methylphenidate as *"a primary pro-dopaminergic, secondary pro-noradrenergic, and tertiary pro-cholinergic mechanism"*.

The main mechanism for the therapeutic effects of methylphenidate is postulated to be its effect on dopamine (Nevels *et al.,* 2013:29; Wilens, 2008:S51). Methylphenidate is an indirect dopamine agonist (Wilens, 2008:S48) that significantly increases the extracellular dopamine concentration, especially in the striatum (Volkow *et al.,* 2001:3). This increase occurs because the *d*-enantiomer (Ding *et al.,* 1997:77; Markowitz & Patrick, 2008:S60) of methylphenidate is a potent inhibitor of the dopamine transporter, DAT (Dresel *et al.,* 2000:1522; Kuczenski & Segal, 1997:2036; Vles *et al.,* 2003:79). DAT is responsible for the clearance of extracellular DA from the synapse after stimulation of the presynaptic dopaminergic neuron (Giacomini & Sugiyama, 2011:116). Consequently, DAT determines both the magnitude and duration of a dopamine signal (Volkow *et al.,* 2005:1410). The inhibition of DAT therefore results in an increase in the extra-neural dopamine concentration. The extra-neural concentration of dopamine is also increased because methylphenidate promotes the release of dopamine from presynaptic dopaminergic neurons (Scahill *et al.,* 2004:85; Volz *et al.,* 2008:167). This increase in extra-neural concentration of dopamine leads to disinhibition of D2-autoreceptors on the presynaptic neuron and activation of D1-receptors on the postsynaptic neuron (Wilens, 2008:S48). It is thought that the striatum is involved in motor selection response and the reward system (Grillner *et al.,* 2005:369). Rosa-Neto and colleagues (2005:874) suggest that these increases in striatal dopamine are associated with the improvement of symptoms such as impulsivity and inattention. The implication of the increased dopamine concentrations and the reward function of the striatum are discussed in paragraph 2.1.6.

The therapeutic effects of methylphenidate are not only believed to stem from improved functioning in the striatum, but also from enhanced functioning in the prefrontal cortex of both dopamine and norepinephrine (Engert & Pruessner, 2008:325). The prefrontal cortex is the area of the brain that is thought to be involved in the regulation of attention (Arnsten, 2009:34). In addition to the blockade of the dopamine transporter, methylphenidate also inhibits the norepinephrine transporter (NET) in humans (Hannestad *et al.,* 2010:858), especially in the prefrontal cortex (Berridge *et al.,* 2006:1118). Evidence from animal studies suggests that the main pathway for dopamine reuptake in the prefrontal cortex is by means of NET and not DAT

(Carboni *et al.,* 1990:1068; Morón *et al.,* 2002:392). The inhibition of NET in the prefrontal cortex may be yet another mechanism that leads to an increase in extra-neural dopamine concentration after methylphenidate administration (Gronier, 2011:202).

### 2.1.4 Indications for methylphenidate

Methylphenidate has been registered for use in attention-deficit/hyperactivity disorder (ADHD) for more than 60 years (Mayes *et al.,* 2008:151). It is also effectively used for narcolepsy (Morgenthaler *et al.,* 2007:1708). Although many other possible indications have been researched, these are the only two registered indications for methylphenidate in South Africa. Methylphenidate is marketed as Methylphenidate Douglas®, Ritalin® (immediate release), Ritalin LA® (extended release) and Concerta® (extended release) in South Africa (Rossiter, 2014:508). Typically the daily dose ranges from 10 mg to a maximum of 60 mg for short-acting preparations and a maximum of 72 mg daily for long-acting preparations (AACAP, 2007:905). Other indications for methylphenidate and the supporting evidence for efficacy are summarised in Table 2-1. Of the many suggested off-label uses for methylphenidate, the indications with the best supporting evidence may be cancer-related fatigue, Parkinson's disease and apathy in Alzheimer's disease (Table 2-1). Unsurprisingly, the pathology of both Parkinson's disease (Meissner *et al.,* 2011:377; Volz *et al.,* 2008:166) and Alzheimer's disease (Mitchell *et al.,* 2011:420) involves deficient dopaminergic activity, which is why methylphenidate, as an inhibitor of DAT and NET, may be a beneficial treatment for these diseases.

The evidence supporting use in cancer-related fatigue is inconclusive. A systematic review (Minton *et al.,* 2010:16) concluded that there is statistically significant merit in using psycho-stimulants for cancer-related fatigue, although a phase III, randomised, double-blind, placebo-controlled trial (Moraska *et al.,* 2010:3677) with 148 participants could not detect an advantage of long-acting methylphenidate over placebo. Another randomised, double-blind, placebo-controlled trial (Roth *et al.,* 2010:5108) (N=32) reported a clinically significant improvement in fatigue; however, the study also reported a high dropout rate due to adverse effects (6/16). The evidence for efficacy in Parkinson's disease is also conflicting. Reports of statistically significant improvement in gait (Moreau *et al.,* 2012:593) are countered by other studies that could not find a statistically significant difference between methylphenidate and placebo (Espay *et al.,* 2011:1260; Nutt *et al.,* 2004:770). Concerning apathy in Alzheimer's disease there seems to be evidence of efficacy; but, while some researchers caution against adverse effects (Mitchell *et al.,* 2011:418) others report minimal side effects (Rosenberg *et al.,* 2013).

**Table 2-1: Proposed off-label indications for methylphenidate with supporting evidence**

| Study | Type of study | Indication | Key findings |
|---|---|---|---|
| Pérez-Mañá *et al.* (2013) | Systematic review (11 studies reviewed; 2 of those studies investigated MPH) | Amphetamine dependence | Neither study found statistical significance between the effectiveness of methylphenidate and placebo. |
| Chemali *et al.* (2012) | Animal study (N=10) | Anaesthesia recovery | Methylphenidate reduced the time to emergence after a single dose of propofol was given from 735 seconds to 448 seconds. It also induced emergence when a continuous dose of propofol was given. More research is required to establish the efficacy of methylphenidate for this indication in humans. |
| Solt *et al.* (2011) | Animal study (N=12) | | Methylphenidate improved respiratory drive and accelerated arousal from isoflurane general anaesthesia. Methylphenidate shows promise in accelerating recovery with respiratory depression after general anaesthesia; however, more research is required to prove efficacy in humans. |
| Mitchell *et al.* (2011) | Review article (10 studies identified: 5 case reports (total N=13), 2 open-label studies (N=27 and 23), a double blind, ABBA design study (N=1) and 2 double-blind randomised controlled trials (N=13 and 145) | Apathy in Alzheimer's disease | All 10 studies reviewed found an improvement in apathy in patients treated with methylphenidate. Methylphenidate appears to be effective in reducing apathy in Alzheimer's disease; however, the authors did raise concern for the adverse effects of methylphenidate since one RCT (N=13) showed considerable drop-out due to adverse effects. |
| Rosenberg *et al.* (2013) | Multicentre, randomised, placebo-controlled trial (N=60) | | Two of the three measured outcomes showed statistically significant improvement of apathy in the treatment group. The treatment group experienced minimal side effects. The results suggest that methylphenidate is effective as treatment for apathy in Alzheimer's disease; however, more research is needed to verify the results. |
| Challman & Lipsky (2000) | Review article (5 double-blind, placebo-controlled trials) | Brain trauma | Three of the five double-blind, placebo-controlled trials reported positive effects while the other two reported methylphenidate had no effect on neural behavioural symptoms after brain injury. The results may be mixed since the trials were conducted at different periods after brain trauma occurred. It is possible that methylphenidate is effective at relieving neural behavioural symptoms immediately after the trauma. More research is needed to provide conclusive evidence of efficacy for this indication. |

**Table 2-1: Proposed off-label indications for methylphenidate with supporting evidence**

| Study | Type of study | Indication | Key findings |
|---|---|---|---|
| Castells *et al.* (2010) | Systematic review (16 studies, three of which considered MPH) | Cocaine dependence | There is no evidence to support the efficacy of methylphenidate in the treatment of cocaine dependence. |
| Gagnon *et al.* (2005) | Prospective clinical trial (N=14) | Delirium | After treatment for hypoactive delirium, cancer patients showed an improvement in symptoms. The reason for the effectiveness of methylphenidate in this trial is unknown and so the phenomenon requires more investigation. |
| Galynker *et al.* (1997) | Prospective clinical trial (open label) (N=27) | Dementia | A decrease was observed in the negative symptoms of dementia. Although methylphenidate appeared to be effective for this indication, blinded, randomised, controlled trials are needed to confirm the results. The authors furthermore note that future research would also require the use of standardised diagnostic criteria. |
| Candy *et al.* (2008) | Systematic review (24 randomised controlled clinical trials, 10 of which observed MPH) | Depression | The quality of the trials was poor and so there is unsatisfactory evidence to support the use of methylphenidate for this indication. The authors suggest that methylphenidate should only be considered if proven antidepressants have failed and short term treatment is required. |
| Abbasowa *et al.* (2013) | Systematic review (18 randomised controlled trials, three specifically pertaining to methylphenidate) | Depression (unipolar depression and bipolar depression) | There is no evidence of the efficacy of methylphenidate for depression. |
| Weissenberger *et al.* (2001) | Case report (N=1) | Familial male precocious puberty | After initiating methylphenidate therapy, the patient displayed a decrease in aggressive and sexual behaviours. More research is needed to confirm the efficacy of methylphenidate for this indication. |
| Minton *et al.* (2010) | Systematic review (four out of five studies reviewed investigated MPH) | Fatigue in cancer | Results from a meta-analysis indicate that there is a statistically significant difference between the efficacy of psychostimulants for cancer-related fatigue over placebo (std. mean difference: 0.28 with a 95% confidence interval of 0.48-0.09 and $p$=0.005). However, the trials used small samples. The authors recommend further study with larger trials to evaluate the results. |

**Table 2-1: Proposed off-label indications for methylphenidate with supporting evidence**

| Study | Type of study | Indication | Key findings |
|---|---|---|---|
| Moraska *et al.* (2010) | Phase III, randomised, double-blind, placebo-controlled trial (N=148) | | Treatment with long-acting methylphenidate did not significantly improve cancer-related fatigue. However, the treatment group did experience more side effects than the control group. The results are not satisfactory evidence to support the efficacy of long-acting methylphenidate in cancer-related fatigue. |
| Roth *et al.* (2010) | Randomised, double-blind, placebo-controlled trial (N=32) | | The treatment group showed clinically significant improvement of fatigue; however, six of the 16 patients in the treatment group withdrew due to cardiac adverse events. There is evidence to support the use of methylphenidate for cancer-related fatigue but the authors caution that patients should be monitored for pulse and blood pressure elevations. |
| Breitbart *et al.* (2001) | Randomised, double-blind, placebo-controlled trial (N=109) | Fatigue in HIV infection | Of patients using methylphenidate, 41% (N=15) showed a clinically significant reduction in fatigue compared to a 15% (N=6) reduction in patients using placebo. It should be noted that out of the 53 patients who started the trial, only 37 completed it. Methylphenidate appears to be more effective at reducing fatigue in HIV patients than placebo. Since the large dropout rate may reduce the credibility of the results, more research is required to verify this conclusion. |
| Induruwa *et al.* (2012) | Review article | Fatigue in multiple sclerosis | Anecdotal evidence and patient reports indicate methylphenidate is effective for fatigue in multiple sclerosis. More research is needed to establish whether the benefit of methylphenidate outweighs the risks of use. |
| McElroy *et al.* (2012) | Review article (five studies reviewed which includes 10 case reports and two trails with a collective pool of 10 patients. Only two of the five studies considered MPH) | Obesity | Some studies have indicated that methylphenidate may have potential for treatment of eating disorders. The use of methylphenidate for this indication merits investigation by a controlled clinical trial. |
| Sher & Reinberg (1996) | Case study (N=7) | Giggle incontinence | Methylphenidate treatment resulted in positive clinical outcomes in all the patients; however, controlled trials are needed to confirm this result. |

**Table 2-1: Proposed off-label indications for methylphenidate with supporting evidence**

| Study | Type of study | Indication | Key findings |
|---|---|---|---|
| Espay *et al.* (2011) | Double-blind, placebo-controlled, randomised trial. (N=27) | Parkinson's disease | The treatment group showed no improvement in gait, marginal improvement in depression and worsened motor-function, sleepiness and quality of life. Despite contradicting data from open label studies, this trial could not prove the efficacy of methylphenidate in improving gait in Parkinsonism. |
| Moreau *et al.* (2012) | Multicentre, parallel, double-blind, placebo-controlled, randomised trial (N=81) | | After treatment with methylphenidate, patients showed an improvement in gait but also experienced more side effects than the control group. The authors advocate the use of methylphenidate in advanced stages of Parkinsonism; however, they acknowledge that the long term risk-benefit ratio must still be established. |
| Nutt *et al.* (2004) | Triple blind, placebo-controlled, randomised trial (N=17) | | On its own, methylphenidate caused no improvement of parkinsonism. However, when combined with levodopa, methylphenidate improved the response to levodopa and reduced the hypotensive effect of levodopa. The results indicate that methylphenidate may have a promising role in the treatment of parkinsonism; however, more research is needed to evaluate the long term effectiveness of methylphenidate for this indication. |
| Johnson *et al.* (1995) | Case study (N=2) | Weaning from mechanical ventilation | Methylphenidate appeared to improve respiratory efforts, alertness, mood and motivation in the two patients which lead to successful weaning from mechanical ventilation after conventional treatments failed. However, the authors concede that without evidence from controlled trials, it is impossible to attribute the weaning unequivocally to methylphenidate. |

HIV= Human immunodeficiency virus
MPH= Methylphenidate
RCT= Randomised controlled trial

### 2.1.5 Adverse effects associated with methylphenidate

Methylphenidate is reasonably safe to use orally and generally well-tolerated when therapeutic doses are taken in the short-term (Godfrey, 2009:202; Klein-Schwartz, 2002:220; Leonard *et al.,* 2004:175; Morton & Stockton, 2000:159). In a review article regarding the safety of therapeutic methylphenidate use in adults, Godfrey (2009:197) found that statistically significant adverse effects identified as attributable to methylphenidate from ten clinical trials included dry mouth (31%), decreased appetite or anorexia (27%), mood liability (18%), nervousness (22%), depression (21%), weight loss (11%) and vertigo (12.5%). Five of the 26 placebo-controlled trials reviewed by Godfrey (2009:197) also reported cardiovascular events, such as increased blood pressure and pulse. In these trials, the number needed to harm (i.e. the number of patients that need to be treated to result in one more patient dropping out of the trial due to adverse events) was 23. The FDA reports that the most common adverse effects are nervousness and insomnia (Gelperin & Phelan, 2006:41). Other common short term adverse effects seen under normal therapeutic conditions include headaches, irritability, anxiety, abdominal pain and palpitations (Klein-Schwartz, 2002:220; Leonard *et al.,* 2004:175; Repantis *et al.,* 2010:203). A rare side effect of methylphenidate is psychosis (Gelperin & Phelan, 2006:41; Kraemer *et al.,* 2010; Mosholder *et al.,* 2009:615).

Not much data is available regarding the long-term safety of methylphenidate. Concerns have been raised that serious cardiovascular side effects and psychosis could occur after years of methylphenidate use (Godfrey, 2009:201). Despite these concerns, data regarding the cardiovascular risks are conflicting. A systematic review by Westover and Halm (2012) concluded that, due to poor power, confounding, and bias, it could not be conclusively deduced that methylphenidate is associated with adverse cardiovascular events such as myocardial infarction, stroke or sudden death. However, Lakhan and Kirchgessner (2012:672) pointed out that this does not necessarily mean that methylphenidate use is not related to less severe cardiac outcomes. With regard to psychosis, there have been reports that methylphenidate causes idiosyncratic psychosis, both in the presence of risk factors (such as a history of drug addiction or vulnerability to psychiatric symptoms) and without. Generally, where cases of psychosis have been reported the symptoms resolved within two days after discontinuation of methylphenidate, although some cases have taken up to seven days (Kraemer *et al.,* 2010; Ross, 2006:1150). According to Ross (2006:1150), manic-like and psychotic-like symptoms may occur in one out of every 400 children treated with methylphenidate. Another concerning characteristic of methylphenidate is its abuse potential. This is discussed in detail in paragraph 2.1.6.

In 2010, there were 31 244 emergency room visits in the United States as a result of ADHD medication use (SAMHSA, 2013a:2). Only 29% of these cases were caused by adverse events, while half of the cases reported were the result of nonmedical use. Concurring with these results, data from a German pharmacovigilance database show 23% of adverse drug reactions related to methylphenidate were a result of methylphenidate abuse. The mean daily dose involved in these cases ranged from 10 mg to 432 mg (Gahr *et al.,* 2014:253). While methylphenidate is fairly well tolerated when used medically, it has been suggested that nonmedical users experience a different side effect profile (Morton & Stockton, 2000:159). For example, Hartung and associates (2013:835) found that students generally experience more side effects when prescription stimulants are used without a prescription or used excessively when compared to students who use prescription stimulants medically. This study reports that students who use prescription stimulants without a prescription were significantly more likely to experience an exaggerated feeling of wellbeing, nervousness and insomnia than medical users (Hartung *et al.,* 2013:835). The authors also found that the former group were less likely to experience weight loss, anxiety and gastro-intestinal problems than medical users.

In another study, researchers found that prevalence of decreased appetite and insomnia in nonmedical users was as high as 74% and 71% respectively (Advokat *et al.,* 2008:602). Rabiner and colleagues (2009a:150) had similar results: in their study the prevalence of decreased appetite and insomnia in nonmedical users was 74% and 63% respectively. These results are much higher than the reported rates for reduced appetite (28%) (Spencer *et al.,* 2005:460) and insomnia (ranging from 19% to 41%) (Epstein *et al.,* 2014:20) found when methylphenidate is used therapeutically. According to Teter *et al.* (2010:297) and Zullig and Divin (2012:895), there is an association between higher rates of depressed mood and nonmedical stimulant use, especially when taken via non-oral routes. Despite the fact that depression is considered a side effect of methylphenidate (Godfrey, 2009:197), Ford and Schroeder (2009:41) theorised that students who experience depressed mood as a result of academic strain are more likely to engage in nonmedical methylphenidate use. However, the cross-sectional nature of all three of these studies (Ford & Schroeder, 2009:41; Teter *et al.,* 2010:297; Zullig & Divin 2012:895) makes the causality of this association impossible to determine. Benson and co-workers (2015:66) suggest that the real association may even lie between ADHD symptoms and depression, rather than depression, being associated with stimulant misuse.

An overdose of methylphenidate typically presents as exasperated sympathomimetic symptoms and particularly cardiovascular and neurological symptoms, for example agitation, euphoria, delusions, psychosis, ventricular tachyarrhythmia, hypertension, movement disorders and seizures, among others (Klein-Schwartz, 2002:220). The clinical presentation of

methylphenidate overdoses is usually moderate (Bruggisser *et al.,* 2011; Klein-Schwartz & McGrath, 2003:293; Spiller *et al.,* 2013:535). Severe toxicity seems to be associated with non-oral administration, such as the intravenous administration of crushed tablets (Bruggisser *et al.,* 2011). Reports of death from methylphenidate overdoses mostly encompass cases that administered the drug intranasally (Massello & Carpenter, 1999:220) or intravenously (Levine *et al.,* 1986:209; Lewman, 1972:68; Parran & Jasinski, 1991:781; Stern *et al.,* 1994:559). Intravenous injection of methylphenidate can lead to the formation of talc and corn starch emboli and granulomatomas in the eyes, lungs, liver, spleen, skin, bone marrow, lymph nodes, and kidneys. These emboli can lead to medullary infarction, pulmonary granulomatosis, pulmonary hypertension, cor pulmonale and retinopathy (AtLee, 1972:49; Bluth & Hanscom, 1981:980; Bruggisser *et al.,* 2011; Gunby, 1979:546; Levine *et al.,* 1986:209; Lewman, 1972:68; Mizutani *et al.,* 1980:427; Parran & Jasinski, 1991:782; Schatz & Drake, 1979:468; Stern *et al.,* 1994:559). Intravenous methylphenidate administration has also allegedly caused hepatic dysfunction (Mehta *et al.,* 1984:151) as well as multiple organ failure (Stecyk *et al.,* 1985:599). Furthermore, there are reports of mycotic femoral artery pseudo-aneurysm as well as severe ischaemia and necrosis following intra-arterial methylphenidate administration (Bruggisser *et al.,* 2011; Still *et al.,* 2001:522).

### 2.1.6 Abuse potential of methylphenidate

The abuse potential of a drug is influenced, *inter alia,* by its availability (Morton & Stockton, 2000:161). There is no doubt that the global availability of stimulants, such as methylphenidate, has been increasing for decades (refer to paragraph 2.2). The global rise in stimulant use, coupled with the fact that methylphenidate increases the dopamine concentration in the reward system of the brain (Clemow & Walker, 2014:66) has lead researchers to the belief that methylphenidate has an abuse potential (Clemow & Walker, 2014:67; Kollins, 2007:38). The first published report of methylphenidate abuse dates as far back as 1960 (Rioux, 1960:348). When assessing a drug's potential for abuse, it is analysed on chemical level (i.e. the degree of chemical similarity with known drugs of abuse), pharmacological level (referring to its pharmacodynamic properties), as well as behavioural level. The last mentioned is normally assessed with regard to (1) its reinforcing effects, (2) its discriminative-stimulus effects and (3) its subjective effects in humans (Kollins *et al.,* 2001:612).

Methylphenidate shares chemical properties and pharmacological properties (such as mechanism of action and potency) with both cocaine and amphetamine. A review conducted by Kollins and associates (2001:623) reported that 71.8% of human studies attest that, based on a behavioural analysis, methylphenidate has an abuse potential similar to that of amphetamine and cocaine. The authors furthermore state that while the reinforcing effects of methylphenidate seem to be dependent on the dose and route of administration, the discriminative-stimulus

effects and the subjective effects were not. Nonetheless it should be noted that methylphenidate abuse, *per se,* is less common than can be expected from its abuse potential. This does not, however, negate the much more common problem of methylphenidate misuse and diversion (Kollins, 2007:40). The considerations and consequences of methylphenidate misuse are discussed in more detail in paragraph 2.5.

In addition to methylphenidate's chemical, pharmacodynamic and behavioural properties that influence its abuse liability, there are several additional factors to consider, such as pharmacokinetics, context and conditioning and formulation. The observation that the reinforcing effects of methylphenidate depend on dose and route of administration can be explained by pharmacokinetics (Volkow & Swanson, 2003:1914). Research has shown that the shorter the onset and duration of action, the larger the potential for abuse (Balster & Bigelow, 2003:S33; Oldendorf, 1992:24). This means that the abuse potential of methylphenidate is higher when it is taken at high doses or via non-oral routes because it results in rapid delivery to the brain and consequently leads to more rapid changes in DAT blockade and a faster accumulation of extra-neural dopamine (Swanson & Volkow, 2003:619; Volkow & Swanson, 2003:1913). This is supported by the observation that reinforcing effects are experienced when methylphenidate is taken intravenously (Volkow *et al.,* 1999:411) and not when it is used at oral therapeutic doses (Volkow *et al.,* 2001:3). The mechanism behind the reinforcing effect seems to be a result of increased dopamine concentrations (Volkow *et al.,* 1999:411) and may also involve an increase in μ-opioid receptor activation via dopamine receptors. Evidence for the involvement of opioid receptors in this mechanism was discovered by Zhu and associates (2011:289), who found that supra-therapeutic doses of methylphenidate increased opioid receptor activity and that the opioid antagonist naltrexone could mitigate the rewarding effects of methylphenidate (Zhu *et al.,* 2011:289). Volkow and Swanson (2003:1916) state that some individuals may be more vulnerable to methylphenidate abuse than others. The authors postulate that methylphenidate's abuse potential is also affected by context and conditioning. For example, the dopamine increase may be amplified when the individual expects a feeling of getting high, whereas it is not necessarily the case when it is used medically. Conversely, a study conducted by Kollins and associates (2009:80) showed that individuals with ADHD experience reinforcing effects at therapeutic doses while individuals without ADHD did not.

The abuse liability of a drug is also influenced by its formulation and the crushability of the tablets (McColl & Sellers, 2006:S52). Sudden drug delivery and short duration of action seems to increase the abuse liability of methylphenidate, leading to the conclusion that long-acting preparations, which result in a longer time required to reach the maximum plasma concentration and with longer half-life, lowers its the abuse liability (McColl & Sellers, 2006:S52; Spencer *et al.,* 2006:391). This assumption is supported by the results from a placebo-controlled,

randomised, double blind, crossover study conducted by Parasrampuria and colleagues (2007:466).

The Ritalin LA® capsules contain a 50:50 mixture of beads. Half of the beads release methylphenidate immediately while the other half are covered in an enteric coat to result in delayed release. The result is two distinct peaks in plasma concentration which are approximately 4 hours apart (Novartis, 2013). Besides having a long half-life and time to reach peak concentration, making it abuse-resistant, Concerta® tablets are also said to be tamper resistant (Coleman *et al.,* 2005:351; DuPont & Lande, 2006:S87; Mastropietro & Omidian, 2013:616). Tamper-resistant formulations reduce abuse liability by making drug extraction from the pharmaceutical product (so that it may be snorted for example) more difficult (McColl & Sellers, 2006:S52). Concerta® has been formulated to release methylphenidate at a controlled rate over 12 hours by using an osmotic release oral system (OROS). The tablet core has three layers which are surrounded by a semipermeable membrane. Around this membrane is a drug overcoat. When swallowed, the outer drug coat disintegrates which results in an immediate-release dose that accounts for approximately one fifth of the total dose (Parasrampuria *et al.,* 2007:460). The partially permeable membrane then allows water to enter the tablet core through osmosis. The tri-layer core consists of two drug layers and an osmotically active layer (containing an osmotic polymer) that swells and slowly pushes the drug out of the core through a small laser drilled hole (Coleman *et al.,* 2005:351). The final result is a slow, gradual increase in plasma concentration that peaks approximately 8 hours after administration (Parasrampuria *et al.,* 2007:462). This drug design hampers intravenous administration because the polymer excipient forms a gel when the crushed tablet comes in contact with water. It also impedes intranasal abuse because, even if the tablets are crushed (which is difficult), it forms irregular fragments which would be difficult to snort. Furthermore once the fragments come in contact with the nasal mucosa, the moisture will result in the formation of a gel.

It should be noted that while extended release formulations may lower the abuse liability, numerous reports confirm that extended-release methylphenidate preparations, such as Concerta®, are certainly not spared from misuse (Advokat *et al.,* 2008:602; Brandt *et al.,* 2014:274; Kroutil *et al.,* 2006:141; McNiel *et al.,* 2011:370; Sembower *et al.,* 2013:35).

### 2.1.7 Contra-indications

Since methylphenidate can aggravate the following conditions, it is contra-indicated in tic disorders, hyperkinetic movement disorders, glaucoma, psychosis, tension, anxiety and agitation (AACAP, 2002:36S; Gelperin & Phelan, 2006:41; Leonard *et al.,* 2004:173; Novartis, 2013). Additionally, it is recommended that patients should be assessed for cardiovascular disease and drug dependence before being prescribed methylphenidate (AACAP, 2002:36S;

Godfrey, 2009:202; Vetter *et al.,* 2008:2416). Due to the elevated risk of a hypertensive crisis, methylphenidate is contra-indicated in concomitant use of monoamine oxidase inhibitors. Methylphenidate should be avoided in pregnancy since animal studies have alluded to a teratogenic potential and there are no controlled clinical studies to support the safe use of methylphenidate during pregnancy (Novartis, 2013).

## 2.2 Epidemiology of methylphenidate use

Global methylphenidate use has increased significantly since the 1990s. According to statistics gathered in 2013 by the International Narcotics Control Board (INCB), methylphenidate manufacturing and use continues to rise, reaching a record-breaking level of 72 tons consumed in 2013 alone. Although the largest methylphenidate consumer worldwide is the USA, South Africa is listed as the ninth largest consumer (in terms of both overall consumption as well as consumption per 1000 inhabitants per day) (INCB, 2014:33). Table 2-2 is a summary of epidemiological studies of methylphenidate and other ADHD medications based on prescription data. These studies have a global distribution and include the following countries: Australia, Canada, Denmark, France, Germany, Iceland, Israel, the Netherlands, New Zealand, Spain, Sweden, Switzerland, the UK and the USA.

Without exception, all the studies listed in Table 2-2 showed that the use of ADHD medication was increasing. One study could be found that did not report an increase in methylphenidate use. This study, conducted by Chai and co-workers (2012:26), found that methylphenidate use by children in the United States remained steady from 2002 until 2010. They reported that the most common ADHD medication used by children was methylphenidate and that it was also the most common drug used by children between the ages of 12 and 17 years (accounting for 4.5% of all prescriptions). However, this study did mention that the use of dexmethylphenidate increased over the time period.

Based on Table 2 2, the annual prevalence growth rate for the ADHD medications and stimulants vary from 9.5% to 60.6% per year. That of methylphenidate in particular varies between 12.0% and 42.9% per year, except for one USA study that only measured extended release methylphenidate and showed an annual prevalence growth rate of 2.8%. In the United Kingdom there was as much as a 96-fold increase in stimulant use in the 10 years from 1992 until 2001 (Hsia & Maclennan, 2009:212). The most drastic growth rates are likely due to low previous prevalence.

While the studies summarised in Table 2-2 are limited to prescription trends of methylphenidate, data from other sources come to the same conclusion. In the USA alone, the annual production quota of methylphenidate (the maximum quantity that may be produced) has risen from

1 361 kg in 1985 to 10 410 kg in 1995, 35 000 kg in 2005 and finally 83 750 kg in 2015 (Drug Enforcement Administration, 2014; Morton & Stockton, 2000:161). McCabe and colleagues (2014:1179) pooled data from five cross-sectional studies spread over ten years and found that both the past year prevalence and the lifetime prevalence of medical use of prescription stimulants by college students have risen. The former increased from 1.9% in 2003 to 4.7% in 2013 and the lifetime prevalence increased from 5.3% to 7.0% in the same time period. Pincus and colleagues (1998:529) analysed visits to healthcare practitioners and reported that the number of visits that resulted in a prescription for stimulant medications rose from 0.57 million in 1985 to 2.86 million in 1994. Data from interviews by the Medical Expenditure Panel Survey spanning over 14 years (1996-2008) was analysed by Zuvekas and Vitiello (2012:162). These authors report the prevalence of ADHD medication use by children increased from 2.4% to 3.5% in this period, giving an annual growth rate of 3.4% per year. Olfson and co-workers (2003:1074) also drew data from the Medical Expenditure Panel Survey and reported that the prevalence of ADHD medication use was a low as 0.9% nine years previously in 1987.

There is little data regarding trends of methylphenidate use in South Africa. An analysis of sales data between 1994 and 1997 in South Africa indicated a rise in methylphenidate use from 145 569 to 179 548 packs of 30 (Crutchley & Temlett, 1999:1076). These authors did a survey where they found 1.65% of children in KwaZulu-Natal, a South African province, used methylphenidate in 1991. A successive analysis of prescription claims data from a study conducted in 2004 indicated that the prevalence of methylphenidate use by children in this province at that time was 2.1% (Truter, 2009:416). Another study that analysed prescription claims from a South African medical aid database reported a national prevalence of 1.8% methylphenidate use by children in 2002 (Truter & Kotze, 2005:82). The study conducted by Truter (2009:414) in 2004 reported 3% of children and adolescents in South Africa received a prescription for methylphenidate in the period of one month in 2004. This prevalence is higher than those reported in European countries, but it is in line with American prevalence rates (refer to Table 2-2) and lower than rates reported in Israel. Overall these studies suggest that the prevalence of methylphenidate use have been increasing in South Africa as well.

Although few studies listed in Table 2-2 specifically reported on methylphenidate use, several of the studies noted that the most common drug of the group measured was methylphenidate (Chai *et al.,* 2010:28; McCarthy *et al.,* 2012; Zito *et al.,* 2003:19) and that it, especially the extended release formulation, was responsible for the majority of the reasons why the consumption of the drug group increased (Geirs *et al.,* 2014:419; Hollingworth *et al.,* 2011:334; Hsia & Maclennan, 2009:212; Treceño *et al.,* 2012:437). According to the utilisation study conducted by Treceño *et al.* (2012:437), there were radical increases in ADHD medication use, as much as 18-fold between the years 2005 and 2009 because of the introduction of extended

release methylphenidate formulations. The authors concluded that there is little evidence that the extended release formulations are more efficacious than immediate release and added that the extended release preparations are much less cost-effective.

In a study conducted in South Africa, only approximately 40% of methylphenidate prescriptions were immediate release, the rest of the prescriptions constituted modified or sustained release (Truter, 2009:415). However, this proportion may have changed since this was measured before Concerta® came onto the market in South Africa.

Generally males use more ADHD medications and methylphenidate than females (Calver *et al.,* 2007:125; Castle *et al.,* 2007:336; Hollingworth *et al.,* 2011:335; Jaber *et al.,* 2014; McCarthy *et al.,* 2012; Truter, 2014:1158; Zuvekas & Vitiello, 2012:163). In spite of this, several studies agree that treatment rates for females are growing more rapidly than for males (Castle *et al.,* 2007:340; Geirs *et al.,* 2014:420; Jaber *et al.,* 2014; Knellwolf *et al.,* 2008:313; McCarthy *et al.,* 2012; Robison *et al.,* 1999:216; Safer *et al.,* 1996:1087; Schubert *et al.,* 2010:616; Zito *et al.,* 2003:21).

Besides gender, age also plays a role in ADHD medication utilisation, but, unlike gender, the degree of use for the different age groups varies across studies. Knellwolf and colleagues (2008:313) found that six to 11 year old children use the most methylphenidate. This finding agrees with the results of Truter (2009:414) who reported most children who use methylphenidate are between the seven and 12 years old. On the other hand, Hollingworth and co-workers (2011:335) concluded that 10-14 year olds used the most methylphenidate. Likewise, Castle and associates (2007:336) state that older children are more likely to use ADHD mediations than younger children but that young adults are more likely than older adults to use ADHD mediations. Geirs and colleagues (2014:419) established that the demographic group that displayed the most rapid surge in ADHD medication use was young adults, aged 19-24 years. Out of the children in their population, Jaber and colleagues (2014) found the largest increases in methylphenidate use in the 14-18 year old age group, as did Schubert and colleagues (2010:616) who observed a five-fold increase in this age group between the years of 2000 and 2007.

Other demographic variables that may play a role in methylphenidate use are ethnicity and socioeconomic status (Jaber *et al.,* 2014; Zuvekas & Vitiello, 2012:163). According to a study conducted by Calver and co-workers (2007:126), adults with the least socioeconomic disadvantage are more likely to receive stimulants while the most socioeconomically disadvantaged children are more likely to receive stimulants than their respective counterparts. The authors also found that people residing in large cities were more likely to use stimulants compared to people living in remote areas.

There is a large geographical variability regarding the volume of prescriptions for ADHD medications such as methylphenidate (Table 2-2). Although the most obvious explanation would be that the prevalence of ADHD varies according to time and/or location, a review of 135 studies from 1985 to 2012 revealed that the prevalence of ADHD has remained constant over the past thirty years and does not vary according to region (Polanczyk *et al.,* 2014:439). More likely explanations for the geographical variation of the quantity of ADHD medication use include different governmental regulations (i.e. stern regulations may limit use), diagnostic criteria, training of medical health care providers, reimbursement regulations, prescribing practices, availability of ADHD medications and varying perceptions of ADHD (Berbatis *et al.,* 2002:542; Geirs *et al.,* 2014:420; Gumy *et al.,* 2010:269; Scheffler *et al.,* 2007:455).

Based on casual observation it can be argued that there seems to be a correlation between governmental regulations and methylphenidate prevalence. Countries with low prevalence rates, for example France, Germany and Australia, seem to have stricter regulations regarding methylphenidate prescription than countries with higher rates, for example the USA. In France, where the prevalence of methylphenidate prescriptions for children has been reported to be 0.18% in 2005, it is law that methylphenidate may only be prescribed in a hospital by a neurologist, psychiatrist or paediatrician. After this initial prescription, other physicians may supply a refill prescription as long for a maximum of one year as the dose and quantity remains the same (Knellwolf *et al.,* 2008:312). In Germany as of September of 2009, methylphenidate may only be prescribed by a behavioural disorder specialist if other measures have failed (Schubert *et al.,* 2010:615). In Australia, where the prescription of methylphenidate is also restricted to specialists, the prevalence of methylphenidate use in children in 2004 was as low as 0.89% (Preen *et al.*, 2007:123). These specialists must furthermore be registered to prescribe stimulants and they may only prescribe these stimulants for ADHD, narcolepsy, brain damage and depression (Calver *et al.,* 2007:124). The United States of America, on the other hand, has no such restrictions. According to federal law, a practitioner (defined as physician, dentist, veterinarian, scientific investigator, pharmacy, hospital or another authorised person) may prescribe methylphenidate within their professional practice (Drug Enforcement Administration, 2006). Some American states have even allowed nurses to prescribe controlled substances such as methylphenidate (Safer & Malever, 2000:537).

Similar to the correlation with governmental regulation, there is also an apparent association between a country's methylphenidate use prevalence and the type of prescribers that prescribe the majority of prescriptions. In 2007 in Germany, where the majority of the prescriptions were written by psychiatrists and paediatricians (31.1% and 37.7%, respectively) and not general practitioners (10.8%), the prevalence of methylphenidate prescriptions was as low as 1.06% (Schubert *et al.,* 2010:618). Geirs and co-workers (2014:419) report that, in 2012, the

prevalence of ADHD medication use by adults in Iceland was 1.2%. These authors also specified that the vast majority of the initial prescriptions were from specialists (79%) and that only 10% and 3%, of the initial prescriptions were written by primary care practitioners and unspecialised doctors respectively. Likewise, the prevalence of methylphenidate use in Switzerland was 1.02% in 2005 and again the majority of the prescriptions were written by paediatricians and psychiatrists, with 87% of the children receiving a prescription from at least one of these specialists at least once a year (Gumy *et al.,* 2010:268). Conversely, a survey conducted in the USA, reporting prevalence rates of methylphenidate use between 8% and 12.5%, stated that 31% of the ADHD diagnoses were made by general practitioners and that they also wrote 54% of the prescriptions for ADHD medications (Advokat *et al.,* 2008:602). A study conducted in South Africa by Truter (2005:61) showed similar results: in her study, 53.4% of the prescriptions for methylphenidate were written by general practitioners. Gumy and colleagues (2010:270) assert that ADHD is a condition that requires specialised training to diagnose and treat. It has been said that family practitioners tend to diagnose ADHD more rapidly and prescribe medication more readily than specialists such as paediatricians and psychiatrists. Furthermore it is also more likely for family practitioners to overlook comorbidities (Ferguson, 2000:186). This could explain why prevalence rates seem to be higher in countries where general practitioners prescribed a large portion of the medications, such as the USA, compared to countries with lower rates such as Germany, Iceland and Switzerland.

Although the exact reported values of the studies discussed in this section are difficult to compare due to differences in methodology and the manner in which results were reported, it is evident that the use of ADHD medications such as methylphenidate has increased globally for the past few decades. Researchers also report that not only is the number of individuals who are prescribed methylphenidate increasing, the amount of methylphenidate consumed per individual is increasing as well (Castle *et al.,* 2007:338; Schubert *et al.,* 2010:618). Reasons for this increase have been suggested to be:

- Improved diagnostic rates of ADHD among children (Olfson *et al.,* 2003:1075; Sembower *et al.,* 2013:35) and adults (Castle *et al.,* 2007:340; Hsia & Maclennan, 2009:213; Sembower *et al.,* 2013:35)
- Increased amounts of girls and adults using methylphenidate (Sciutto & Eisenberg, 2007:111; Safer *et al.,* 1996:1087)
- Increased public awareness of ADHD (Castle *et al.,* 2007:340; Geirs *et al.,* 2014:420; Hollingworth *et al.,* 2011:335; Olfson *et al.,* 2003:1075; Polanczyk *et al.,* 2014)
- More optimistic public image of ADHD treatments (Safer *et al.,* 1996:1087)
- Increased popularity of long-acting methylphenidate (Hollingworth *et al.,* 2011:334)

- Increased availability of ADHD drugs including methylphenidate (Geirs *et al.,* 2014:420; Hsia & Maclennan, 2009:213; Polanczyk *et al.,* 2014)
- Marketing by pharmaceutical companies (Graf *et al.,* 2014; Hollingworth *et al.,* 2011:335)
- Improved patient compliance (Castle *et al.,* 2007:341)
- Societal changes (Hollingworth *et al.,* 2011:335)
- Changed recommended clinical practice (Polanczyk *et al.,* 2014) and the diagnosis of more mild/ambiguous cases (Graf *et al.,* 2014)

Despite these plausible reasons, researchers still express concern over the increase in methylphenidate use. Some suggest that it may be an indicator of inappropriate prescribing (Angold *et al.,* 2000:983; Graf *et al.,* 2014). Others have raised the concern that it may be associated with non-indicated use such as improving cognitive enhancement (Graf *et al.,* 2014; Schubert *et al.,* 2010:620). Klein-Schwartz (2002:219) further cautions that abuse rates are likely to increase as therapeutic use increases.

**Table 2-2: Prescription prevalence studies of stimulants, ADHD medications and methylphenidate from the past three decades**

| Study | Study period | Location | Study population | Drug measured | Annual prevalence of drug(s) used from the start of the study period to end of the study period | Relative increase in prevalence over time period | Annual prevalence growth rate (%)*** |
|---|---|---|---|---|---|---|---|
| Berbatis *et al.* (2002) | 1994-2000 | Australia, Canada, Denmark, France, the Netherlands, New Zealand, Spain, Sweden, the UK and the USA | Unclear | Psychostimulants (dexamphetamine and MPH) | | 45% (USA),<br>93% (Canada)<br>87% (the remaining countries) | 12** (all the countries) |
| Castle *et al.* (2007) | 2000-2005 (6 years) | USA | Children (0-19 years) and adults (>20 years) | ADHD medications | 2.8% to 4.4% (children)<br>0.4% to 0.8% (adults) | 57.1%* (children)<br>100%* (adults) | 9.5** (children)<br>15.3** (adults) |
| Geirs *et al.* (2014) | 2003-2012 (10 years) | Iceland | Entire national adult population (>19 years old) | ADHD medications (amphetamine, MPH and atomoxetine) | 0.2% to 1.2% | 500%* | 50 |
| Gumy *et al.* (2010) | 2002-2005 | Switzerland (Canton of Vaud) | School-aged children (5-14 years old) | MPH | 0.74% to 1.02% | 37.83% | 12.6** |

**Table 2-2: Prescription prevalence studies of stimulants, ADHD medications and methylphenidate from the past three decades**

| Study | Study period | Location | Study population | Drug measured | Annual prevalence of drug(s) used from the start of the study period to end of the study period | Relative increase in prevalence over time period | Annual prevalence growth rate (%)*** |
|---|---|---|---|---|---|---|---|
| Hollingworth *et al.* (2011) | 2002-2009 | Australia | Children, youth and adults | Psycho-stimulants (dexamphetamine and MPH) | 2.93 to 5.47 DDD/1000 population/day (psycho-stimulants)<br>0.45 to 1.81 DDD/1000 population/day (MPH) | 87% (psycho-stimulants)<br>300%* (MPH) | 11** (psychostimulants)<br>42.85 (MPH) |
| Jaber *et al.* (2014) | 2005-2011 | Israel | Children (6-18 years) | MPH | 4.2% to 7.5% | 85% | 14.1 |
| Knellwolf *et al.* (2008) | 2003-2005 (3 years) | France | Children and adolescents (6-18 years) | MPH | 0.11% to 0.18% | 63.5% | 21.2 |
| McCarthy *et al.* (2012) | 2003-2008 (6 years) | UK | Children (6-12 years), adolescents (13-17 years) and adults (>18 years) | ADHD medications (MPH, dexamphetamine or atomoxetine) | 0.48% to 0.92% (children)<br>0.36% to 0.74% (adolescents)<br>0.03% to 0.11% (18-24 years)<br>The prevalence in older age groups was negligible. | 91.7%* (children)<br>105.0%* (adolescents)<br>266.7%* (18-24 years) | 15.3 (children)<br>17.5 (adolescents)<br>44.5 (18-24 years) |

**Table 2-2: Prescription prevalence studies of stimulants, ADHD medications and methylphenidate from the past three decades**

| Study | Study period | Location | Study population | Drug measured | Annual prevalence of drug(s) used from the start of the study period to end of the study period | Relative increase in prevalence over time period | Annual prevalence growth rate (%)*** |
|---|---|---|---|---|---|---|---|
| Robison *et al.* (1999) | 1990-1995 (6 years) | USA | Children (5-18 years) | MPH | 1.06% to 2.79% | 160.4%* | 26.7 |
| Schubert *et al.* (2010) | 2000-2007 (8 years) | Germany (state of Hesse) | Children and adolescents (0-18) | MPH | 0.54% to 1.06% | 96% | 12 |
| Sembower *et al.* (2013) | 2007-2011 (4 years) | USA | Estimates of entire population | Extended-release MPH | | 11.3% | 2.8 |
| Treceño *et al.* (2012) | 1992-2009 (18 years) | Spain (Castilla y León) | Ages unspecified | ADHD medication (amphetamine, dexamphetamine, MPH, modafinil, atomoxetine, and pemoline) | 0.1 DDD/1000 inhabitants/day to 1.5 DDD/1000 inhabitants/day | 1400*% | 77.8 |

**Table 2-2: Prescription prevalence studies of stimulants, ADHD medications and methylphenidate from the past three decades**

| Study | Study period | Location | Study population | Drug measured | Annual prevalence of drug(s) used from the start of the study period to end of the study period | Relative increase in prevalence over time period | Annual prevalence growth rate (%)*** |
|---|---|---|---|---|---|---|---|
| Zito *et al.* (2003) | 1987-1996 (10 years) | USA (north-western region, a Mid-Atlantic state and a Midwestern state) | Children and adolescents (<20 years old) | Stimulants (MPH, amphetamines, and pemoline) | 1.43% to 3.84% (Mid-Atlantic state)<br>1.01% to 3.72% (Midwestern state)<br>0.36% to 2.54% (north-eastern HMO) | 168.5%* (Mid-Atlantic state)<br>268.3%* (Midwestern state)<br>605.5%* (HMO north-western region)<br>For MPH: 2.5-fold to 3.7-fold for Medicaid youths and 7.2-fold for HMO youths | 16.9% (Mid-Atlantic state)<br>26.8% (Midwestern state)<br>60.6% (HMO north-western region) |

* Calculated as follows: [(annual prevalence of last year - annual prevalence of first year)/annual prevalence of first year] *100.
** Reported value.
*** Annual prevalence growth rate calculated as follows (except were indicated by **) = relative increase in prevalence over the time period /length of the time period.

ADHD = Attention-deficit/hyperactivity disorder
DDD = Defined daily dose
HMO = The data originates from a health maintenance organisation
MPH = Methylphenidate
UK = United Kingdom
USA = United States of America

### 2.2.1 Nonmedical use of methylphenidate and similar drugs

The nonmedical use of prescription drugs is common place for a significant proportion of students at universities (Benotsch *et al.,* 2011:154). One study found that as many as 72.8% of students who use prescription drugs non-medically are using prescription stimulants (Brandt *et al.,* 2014:274). For the purpose of this study, nonmedical use is defined as the use of methylphenidate for any reason by a person to whom the drug was not prescribed and/or the incorrect use of methylphenidate (e.g. for inappropriate reasons and/or excessive use of methylphenidate). Other studies have used similar definitions, some including and some excluding the "excessive use of one's own medication" in this definition. There is a lack of consensus when it comes to terminology in this field (Smith *et al.,* 2013:2288). Other terms that have been similarly defined to describe this problem and that are used interchangeably are "misuse", "abuse", "illicit use" and "recreational use". It should be noted that even in the broader definition of nonmedical use, the concept is not the same as "off-label" use, which can be defined as the use of a product in a manner that deviates from the authorised product information (European Medicines Agency, 2014:22; WHO, 2009:21). Off-label use occurs, for example, when the prescriber has no viable registered medications with which to treat a specific condition (WHO, 2009:21). The critical difference in off-label use is that the therapy is prompted and monitored by an authorised prescriber and not the individual.

It has been argued that that availability is central to the degree to which a drug is used in nonmedical ways (Checton & Greene, 2011:261; Morton & Stockton, 2000:161; Novak *et al.,* 2007; Singh *et al.,* 2014). It is therefore concerning that, as reasoned in the previous section, the availability of methylphenidate has increased so dramatically. Researchers have proclaimed this to be, at least partially, the reason for increased cases of nonmedical use, abuse and overdoses (Peralta & Steele, 2010:882; Spiller *et al.,* 2013:532).

The link between medical and nonmedical use of prescription stimulants may be even more direct than due to increased availability. According to McCabe and associates (2014:1181), students with a history of medical use of prescription stimulants are at a higher risk of nonmedical use. For example, according to Novak and co-workers (2007), the odds of someone engaging in nonmedical use of ADHD medication is 22 times higher for someone who has had a valid prescription for ADHD for one year than for someone without a prescription. A meta-analysis of 30 studies concluded that samples that consisted of larger proportions of individuals with ADHD also had higher rates of stimulant misuse (Benson *et al.,* 2015:60). McCarty (2007:1505) argues that an increased social acceptance of prescription drugs and the perception that prescription drugs are safe (compared to illicit drugs), especially among young adults, may also serve as reasons why the misuse of prescription drugs has increased. Results from a qualitative study revealed that some students think methylphenidate must be a safe drug

since it is given to children (Forlini & Racine, 2012:615). Another study showed that while 72% of students perceive cocaine use to be very risky, only 25% had this perception with regard to prescription stimulants (Arria, Caldeira, Vincent, *et al.,* 2008:196). This finding is supported by Looby and co-workers (2014:1102) who also found that students have more positive attitudes to prescription stimulant use than cocaine. Their study pointed out that while the use of cocaine has decreased in recent years, nonmedical prescription stimulant use has surpassed cocaine use.

Researchers have suggested that nonmedical use of methylphenidate and other prescription stimulants may be more common than medical use (Arria, Caldeira, O'Grady, Vincent, Johnson, *et al.*, 2008:165; McCabe *et al.,* 2006a:272; Rozenbroek & Rothstein, 2011:362; Silveira *et al.,* 2014:105). The ratio of nonmedical to medical use was reportedly as high as 5:1 (Arria, Caldeira, O'Grady, Vincent, Johnson, *et al.*, 2008:165) and 2.5:1 (McCabe and co-workers 2006a:272).

Whether nonmedical use of prescription stimulants has increased in recent years is contested. Admitting that trend data for stimulant misuse is lacking (especially outside of the United States), Kaye and Drake (2012:472) asserted that there is insufficient evidence to conclude that the nonmedical use of prescription stimulants has increased in conjunction with increased prescription practices. The authors refer to studies such as the National Survey on Drug Use and Health (SAMHSA, 2014a:65) and the Monitoring the Future Study (Johnston *et al.,* 2013:15). According to these two studies the nonmedical use of prescription stimulants and Ritalin®, respectively, have remained stable in recent years. However, a limitation to the Monitoring the Future Study is that it only measures Ritalin® and not all methylphenidate-containing products. There is at least one national study from the USA that reached the opposite conclusion. McCabe and colleges (2014:1178) estimated that the lifetime prevalence of nonmedical use of prescription stimulants by students have increased from 8.1% in 2003 to 12.7% in 2013. The past-year prevalence increased from 5.4% to 9.3% over the same time period. The increase in nonmedical use and diversion appears to parallel the increase in therapeutic stimulant use.

#### 2.2.1.1 Prevalence of nonmedical use of methylphenidate and similar drugs

Regardless of whether the nonmedical use of prescription stimulants such as methylphenidate has increased or remained stable, the fact is nonmedical use is currently a problem in universities around the world (Table 5-1). This problem will now be discussed in detail, with specific regard to the prevalence, risk factors, reasons for nonmedical use, and nonmedical use behaviours.

The nonmedical use of methylphenidate has been studied since the late 1990s. Studies have either looked at the nonmedical use of methylphenidate on its own, or as a part of a group of medications such as ADHD medications, cognitive enhancers or prescription stimulants. The vast majority of these reports come from the United States; however, reports of nonmedical use have also come from Australia, Europe (Belgium, France, Germany, Ireland, Italy, Netherlands, Switzerland and the UK) as well as the Middle East (Iran) (Table 5-1). Despite the extensive pool of research regarding this matter, little research has been published of South Africa or Africa.

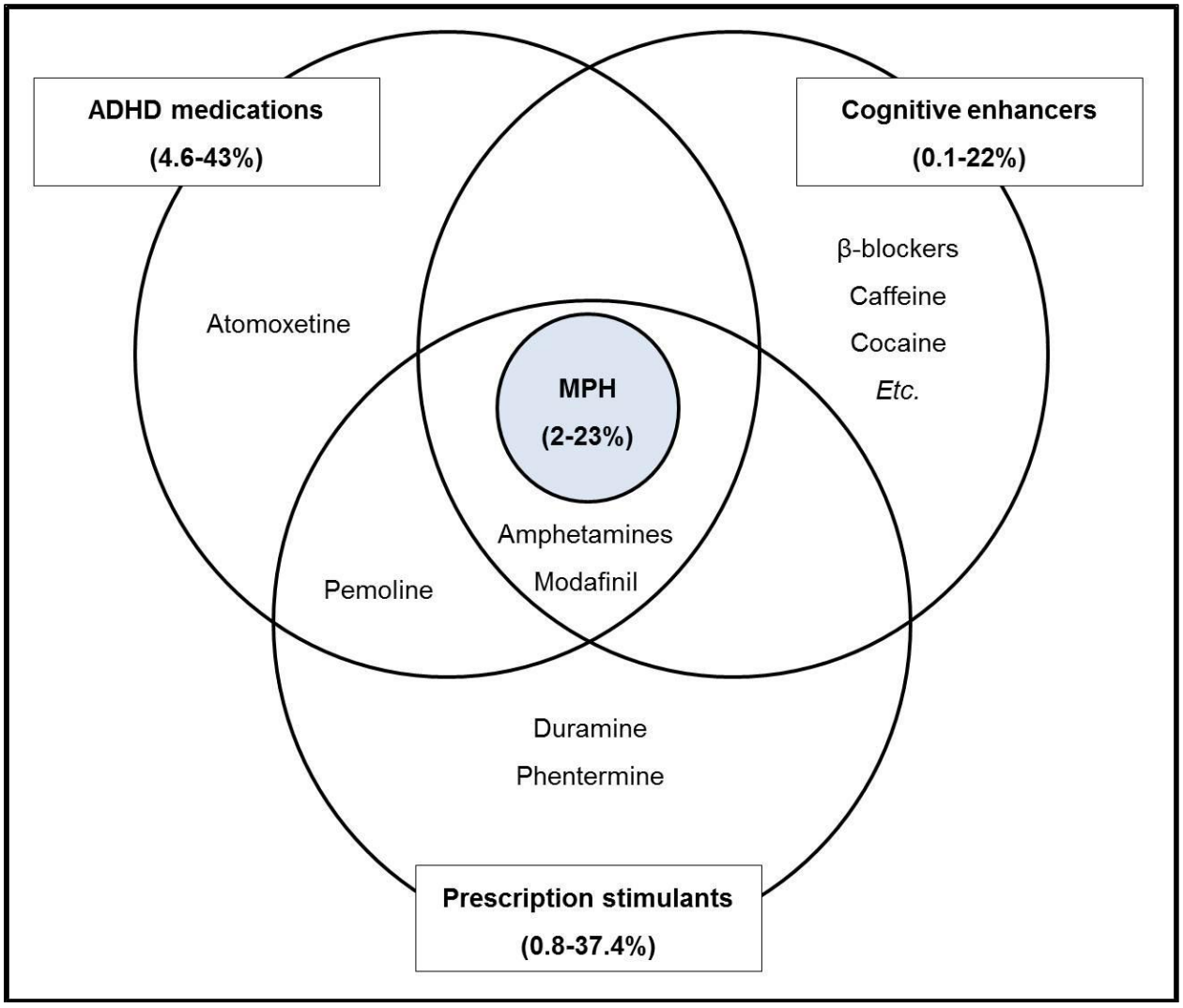


**Figure 2-1: The composition and lifetime prevalence of nonmedical use of methylphenidate, ADHD medications, cognitive enhancers and prescription stimulants**

Figure 2-1 is a representation of drugs that can be considered as ADHD medications, cognitive enhancers and/or prescription stimulants. Researchers, however, do not necessarily always include all of the drugs in each of the respective groups or even all the products containing a

specific drug (even after accounting for differences in brand names between countries). A summary of the specified drugs and their products investigated in each of the studies from Table 5-1 are given in Table 5-2, Table 5-3, Table 5-4 and Table 5-5 in Annexure A. These tables not only show considerable discrepancy between the drugs measured but also strong similarity between the drugs considered to be “ADHD medications” and “prescription stimulants”. Furthermore there is also considerable discrepancy regarding the most common drug and product preferred between these studies. Among the cognitive enhancers, several studies agree that methylphenidate is the most prevalent drug used (Maher, 2008:674; Maier *et al.,* 2013). With regard to the group “prescription stimulants”, one study reports that the favoured stimulant is ephedrine (Holloway & Bennett, 2012:140). Other researchers concluded that the most popular prescription stimulant is Adderall® (dextroamphetamine and amphetamine), with nonmedical usage rates between 75% and 81% and that of Ritalin® varying between 17% and 50% (Brandt *et al.,* 2014:274; Emanuel *et al.,* 2013:1030; McNiel *et al.,* 2011:370). On the other hand, other researches contend that methylphenidate use is more common. White and colleagues (2006:264) report that in their study 96% of the participants used Ritalin® while only 2% used Adderall®. Similar results were found by Zito *et al.* (2003:19).

Ritalin® seems to be the most popular methylphenidate product although Concerta® is certainly not exempt from misuse. Concerta® is used non-medically between 3 and 21.7% of the time (Advokat *et al.,* 2008:602; Brandt *et al.,* 2014:274; McNiel *et al.,* 2011:370). In the study conducted by Advokat and co-workers (2008:602), students used Concerta® (12.5%) non-medically more often than Ritalin® (8%). A different study reports that a larger number of extended release pills for ADHD are diverted than immediate release pills (Aldridge *et al.,* 2011:630).

A recent meta-analysis of 30 studies revealed that the lifetime prevalence of the nonmedical use of prescription stimulants by college students is 17% (95% CI 13-23%) (Benson *et al.,* 2015:60). Figure 2-1 displays the lifetime prevalence of nonmedical use of methylphenidate (2-23%), cognitive enhancers (0.1-22%), ADHD medications (4.6-43%), and prescription stimulants (0.8-37.4%) as determined from the 77 studies summarised in Table 5-1. The past year prevalence of these drugs is 1.4-16% (methylphenidate), 3.2-20% (cognitive enhancers) and 0.2-35% (prescription stimulants). Only one study commented on the past year prevalence of ADHD medications, reporting it to be 4.6% (Novak *et al.,* 2007). Past month use of methylphenidate was reportedly between 2.6% and 8.5% while that of prescription stimulants was between 0 and 12%. No studies measured the past month prevalence of ADHD medications and only one study (Sattler & Wiegel, 2013:224) reported the past month use of cognitive enhancers (1.15%).

Considering the tables in Annexure A, it seems that the prevalence rates for ADHD medications and prescription stimulants should be comparable since the products studied under these names are often identical. This statement is furthermore supported by the fact that these groups have similar prevalence rates. Cognitive enhancers, however, are more difficult to compare. Studies of cognitive enhancers are limited because they measure a wider variety of drugs and generally only measure drugs that were used for the purpose of cognitive enhancement in their prevalence reports (as opposed to recreational use). To illustrate this difference, one study reported the results as both general nonmedical use (4%) of prescription drugs (methylphenidate, modafinil, rivastigmine and β-blockers) and nonmedical use for cognitive enhancement only (3.2%). The part of these rates that is made up by methylphenidate alone is 2.8% and 2.5%, respectively (Schelle *et al.,* 2015). Another study (Singh *et al.,* 2014) found the lifetime prevalence of nonmedical use of methylphenidate to be 5.9%, while the nonmedical use for cognitive enhancement was 4%.

Besides the 77 studies summarised in Table 5-1, the prevalence of methylphenidate and similar drugs was reported in other studies and are worth mentioning. These studies measured the prevalence of nonmedical drug use by medical users, the prevalence of drug use during the students' time at university, and the prevalence among the general population and health care workers.

"Medical users" are those individuals who have a medical reason for using ADHD medications (e.g. they have been diagnosed with ADHD). Despite the fact that some studies consider medical and nonmedical users to be mutually exclusive, others recognise that medical users can also use their medication in a nonmedical manner. Although studies use different definitions, it has been said that these medical users engage in nonmedical use when they use excessive amounts of their own medication, use their own medication for other reasons than the prescribed reason (e.g. to get high), intentionally use the ADHD drug with alcohol or other drugs, administer the drugs via non-oral routes or when they use someone else's prescription medication. In general the prevalence of nonmedical use of ADHD medications among medical users is between 10% and 60% (Gallucci *et al.,* 2014:183; Gallucci, Martin, Beaujean, *et al.,* 2015:222; McNiel *et al.,* 2011:369; Rabiner *et al.,* 2009a:148; Sepúlveda *et al.,* 2011:555; Tuttle *et al.,* 2010:221; Underhill & Langdon, 2013:13; Upadhyaya *et al.,* 2005:803; Wilens *et al.,* 2006:411). According to the study conducted by Sepúlveda and co-workers (2011:555) where 40% of the medical users used their prescribed ADHD medication in a nonmedical manner, 35.8% used the medication excessively, 9.4% used it with the intention to get high, and 18.9% intentionally used the medication with alcohol or other drugs. Regarding the nonmedical use of methylphenidate specifically, prevalence rates of 29% (Darredeau *et al.,* 2007:531) and 33% (Maier *et al.,* 2013) have been reported. Interestingly, in a national study of 4 572 high school

seniors, McCabe and West (2013:1274) discovered that, out of the sample of medical users, 22.9% engaged in medical use before engaging in nonmedical use while 17.8% engaged in nonmedical use before medical use.

Studies have noted that the nonmedical use of methylphenidate and similar drugs is prevalent among young adults (Novak *et al.,* 2007; Sweeney *et al.,* 2013:6), as well as college students (Herman-Stahl *et al.,* 2007:1012; Huang *et al.,* 2006:1066; Wu *et al.,* 2007:199). The average age of initiation in nonmedical use of prescription stimulants has been reported as between 19.5 and 21.6 years (Huang *et al.,* 2006:1066; SAMHSA, 2014a:59; Sweeney *et al.,* 2013:7), whereas that of methylphenidate specifically has been reported as 18.5 years (Barrett *et al.,* 2006:257). Based on these reasons, a reasonable deduction is that most students start using methylphenidate and similar drugs whilst at university. This interpretation is supported by several studies (Arria, Caldeira, O'Grady, Vincent, Fitzelle, *et al.,* 2008:31; Emanuel *et al.,* 2013:1030; McNiel *et al.,* 2011:371; Micoulaud-Franchi *et al.,* 2014:1876; Teter *et al.,* 2003:612; Teter *et al.,* 2006:1504). For instance, a study conducted in 2007 investigating 3 407 sophomore students in the USA revealed that 5.3% of students started taking prescription stimulants during university (Rabiner *et al.,* 2010:643). In contrast, two smaller, more recent studies from America, conducted in 2011 (Bavarian, 2012:100) and 2013 (Bavarian, Flay, Ketcham, *et al.,* 2014:195), reported that 26% and 18% of the students, respectively, started using prescription stimulants during their college years. Volger and associates (2014:160) found this prevalence to be 8.8% among 407 pharmacy students, and it has been reported that 15.2% of medical students use prescription stimulants non-medically during medical school (Wasserman *et al.,* 2014:649). In accordance more than 80% of the medical students who used methylphenidate non-medically (total prevalence of nonmedical users=23%) in another study only started doing so in college (Silveira *et al.,* 2014:104). In a national survey in the Netherlands, the prevalence of the nonmedical use of methylphenidate during the participants' time at university was 2.8% (Schelle *et al.,* 2015).

Prescription stimulants are mostly used non-medically for academic reasons (Benson *et al.,* 2015:62), however, nonmedical use might not cease after students complete university. Emanuel and colleagues (2013:1032) discovered that 17% of the medical students in their study who were using psychostimulants non-medically agreed that they would probably/definitely still be using these drugs in five years' time. Underhill and Langdon (2013:16) reported that 7% of their illicit users planned to continue the illicit use past graduation. The authors furthermore found that not only does illicit use of stimulants continue after graduation, but that students who did not foresee continuing illicit use do continue to do so as alumni.

As for the adult population, there is considerable disagreement about the prevalence of nonmedical use of methylphenidate and related substances. In a study in the US, 30% of

alumni reported using prescription stimulants illicitly in their life time (Underhill & Langdon, 2013:14). Another American study of 4 297 adults found a lifetime prevalence of nonmedical use of prescription stimulants of 7% and that of methylphenidate, specifically, of 4.2%. The past year use was found to be 2% and 0.57%, respectively (Novak *et al.,* 2007). In Australia, Partridge and co-workers (2012:83) concluded that a mere 2.4% of the general public had used a prescription drug to improve concentration/alertness. Similarly, a survey of young men in Switzerland revealed that past year use of Ritalin®, Adderall® and Concerta® for cognitive enhancement was 2% (Deline *et al.,* 2014:3039). On the other hand, according to an international poll of 1 400 participants from 60 countries, as many as one out of five people use drugs such as methylphenidate, modafinil or β-blockers non-medically with the purpose of improving focus, concentration or memory (Maher, 2008:674).

Recent results from the 2013-National Survey on Drug Use and Health (NSDUH) in the USA reported the lifetime use of various stimulants (including methylphenidate, amphetamines, methamphetamine, phentermine, etc.) in young adults aged 18-25 years to be 9.4% and that of adults aged 25 years and older, 8.8%. Interestingly the past year prevalence of young adults was 3.7%, while the past year prevalence of older adults was only 0.9% (SAMHSA, 2013b). This finding suggests that the relatively high lifetime prevalence is not due to current use. Another study stated the nonmedical use of prescription stimulants by youths aged 16-25 years (N=24 409) as 7.6% (Wu *et al.,* 2007:199).

According to the 2013-NSDUH survey (SAMHSA, 2013b), the nonmedical use of stimulants is even present in adolescents (lifetime prevalence = 1.8%; and past year prevalence = 1.1%). These results agree with that of Kroutil and associates (2006:137) who reported 2.6% of persons aged 12-17 years and 5.9% of persons aged 18-25 years had used ADHD stimulants non-medically. This finding corresponds with the results of another study that concluded the lifetime prevalence of nonmedical stimulant use by secondary school students is 2.4% (McCabe *et al.,* 2007:79). A Canadian study that was conducted in 2002 found as many as 6.6% of high school pupils used methylphenidate non-medically (Poulin, 2007:743), and the large national Monitoring the Future Study (2002-2006) revealed a lifetime prevalence of nonmedical prescription stimulant use of 11.2% among high school seniors (McCabe *et al.,* 2015:45).

In short, the nonmedical use of methylphenidate and similar drugs is a documented phenomenon among adolescents, college students as well as the general public. What is arguably most concerning is the fact that there have been reports that healthcare workers are also engaging in nonmedical use of these drugs. Studies show that 11% of psychiatrists and physicians in psychiatry (Timmer & Glas, 2012) and 19.9% of surgeons (Franke *et al.,* 2013) have used drugs for cognitive enhancement. In other studies, as many as 22.2% of physicians admitted to using methylphenidate non-medically (Bulbul *et al.,* 2014:136) whilst 10.9% of

nurses and 15.8% of pharmacists admitted to using stimulants for nonmedical reasons (Kenna & Wood, 2004:925).

Regardless of the population group considered, there is considerable disparity between the reported prevalence rates. In a meta-analysis of 30 studies (Benson *et al.,* 2015:60), the authors concluded that four variables played a significant role in explaining the differences between prevalence rates. First of these variables is study design: longitudinal studies uncover larger prevalence rates than cross-sectional studies. Secondly the prevalence rates are larger when studies measure lifetime use compared to past month use. Thirdly the proportion of students in the sample that have a diagnosis of ADHD was found to be directly proportional to the reported prevalence rate of nonmedical use. Fourthly and finally, larger sample sizes tend to yield marginally more modest prevalence rates (Benson *et al.,* 2015:60).

Other researchers have also suggested that geographical location plays an important role in the discrepancy between prevalence rates (Bavarian, Flay & Smit, 2014:142; Benson *et al.,* 2015:60; Huang *et al.,* 2006:1066; McCabe *et al.,* 2005:101). For example, it can be deduced from Table 5-1 that prevalence rates seem to be higher in the USA than in Europe. However, authors do not always agree on specifics. In the USA, some researchers claim the highest prevalence rates are found in the northeast of the country (McCabe *et al.*, 2005:101), others state high prevalence rates are consistently found in the west (Huang *et al.*, 2006:1066) while another study insists the nonmedical use of prescription stimulants is 2.68 times more likely in the south than in the west (Bavarian, Flay & Smit, 2014:142).

Another factor that clearly has an impact on the diversity of the prevalence rates is differences in definition of the concept nonmedical use. Arria, Caldeira, O'Grady, Vincent, Johnson and associates (2008:164) demonstrate that if the definition is changed from using someone else's prescription stimulants, to one that also includes the excessive use of one's own medication, the prevalence in their study more than doubles from 15.6% to 33.3%. Similarly, in another study the prevalence of nonmedical use of cognitive enhancers (whether or not the individual had a prescription) was calculated as 4%. However, if participants with a prescription for the drug are excluded from the definition, the prevalence rate drops to 2.4% (Schelle *et al.,* 2015).

Several other reasons for these differences have been suggested, some of which include:

- Differences in peer pressure between universities (Singh *et al.,* 2014).
- Competitive academic features of the college or university (Benson *et al.,* 2015:60; McCabe *et al.,* 2005:101).
- Nature of the questionnaire (web-based or paper questionnaire) (McCabe *et al.,* 2006a:276).

- Survey technique (direct survey technique *vs.* randomised response technique) (Dietz *et al.,* 2013:48).

#### 2.2.1.2 Risk factors of nonmedical use of methylphenidate and similar drugs

Substantial effort has been put into identifying risk factors associated with nonmedical use of methylphenidate and related substances. The main factors that have been investigated include gender, ethnicity, sorority/fraternity affiliation, academic achievement and the use of alcohol and other illicit substances. As far as gender goes, the data is divided. Thirty one studies found no difference between men and women when it comes to the nonmedical use of methylphenidate or related drugs. Another 28 studies contend that there is a difference: 26 of these studies hold that men use methylphenidate and related drugs in nonmedical ways more frequently than women (fourteen of those reported a *p*-value of less than 0.01) and two studies found it to be the other way around. Six of the nine studies that measured methylphenidate only state that men are more likely to engage in the nonmedical use of methylphenidate than women (Table 5-6). For example, according to Maier and colleagues (2013) men are twice as likely as women to use methylphenidate in a nonmedical manner. Another study revealed that in a population of medical students, 12.9% of males had used methylphenidate compared to a scarce 2.1% of females (Eslami *et al.,* 2014:46). Since most studies either concluded there is no difference in gender or that men use methylphenidate and similar drugs more often, and since so few studies concluded that women use these drugs more than men, it would seem plausible that the results lean toward men being more at risk of using these drugs non-medically than women. It may also be possible that the ratio of men to women who use prescription stimulants may vary over time since the Monitoring the Future Study shows that this ratio equalised in 2011 (Johnston *et al.,* 2013:144).

As shown in Table 5-7, the data are also split when it comes to ethnicity as a risk factor. Eighteen out of 29 studies state Caucasians are more at risk of nonmedical use of methylphenidate and related substances, while the rest of the studies assert there is no association. Interestingly, one study observed that ethnicity could predict lifetime nonmedical prescription stimulant use but not current use (Gallucci *et al.,* 2014:184,186).

Table 5-7 shows that 14 of 22 studies agreed that being in a sorority or fraternity is also a risk factor for nonmedical use of methylphenidate, prescription stimulants, ADHD medications or cognitive enhancers. Of the remaining eight studies, only one found that belonging to a fraternity is a protective factor whereas seven found no association.

When it comes to academic achievement, most studies (14/19) agree that a lower grade average is another risk factor of nonmedical use, despite the fact that the reported reason for nonmedical use is, more often than not, academic (refer to paragraph 2.2.1.3). According to one

of these studies the odds of a student with low grades to report nonmedical use of prescription stimulants in the past year were up to 2.5 times higher ($p$<0.001) than someone with high grades (Lord *et al.,* 2009:523). It has been suggested that low grades can lead to deviant coping mechanisms since low grades may be perceived as being unjust and may additionally be associated with low social control (Ford & Schroeder, 2009:43). Benson and co-workers (2015:64) suggest the following three reasons for this association: (1) nonmedical stimulant use is ineffective at improving academic outcomes (this assumption is evaluated in section 2.5.3); (2) the poor academic achievers turn to nonmedical stimulant use to improve their academics; and finally (3) other factors, such as ADHD symptomatology, may contribute to poor academic performance in addition to a need for self-medication of symptoms.

Even more studies are in consensus when it comes to the correlation between alcohol use (e.g. binge drinking) and nonmedical use of these drugs. Of the 26 studies that investigated alcohol use, especially excessive alcohol use, as a risk factor for nonmedical drug use, only one could not find an association. In fact, according to a meta-analysis, the odds ratio of engaging in problematic alcohol use and misusing prescription stimulants was 4.7 (95% CI, 2.14-10.15, $p$<001) (Benson *et al.,* 2015:67).

There is also a strong correlation between nonmedical use of methylphenidate and similar drugs and broader substance misuse. Table 5-7 lists 29 papers that report an association with the misuse of at least one other drug. This list not only includes “hard drugs” such as ecstasy, cocaine and lysergic acid diethylamide (LSD) but also the illicit use of prescription pain medication and prescription tranquilisers. The one meta-analysis revealed that the odds of a marijuana user engaging in nonmedical prescription stimulant use was 2.8 times higher compared to those who did not use marijuana (Benson *et al.,* 2015:67). A study that investigated this risk factor reports 72% of nonmedical prescription stimulant users have also used marijuana, compared to a scant 25% of non-users who admit lifetime use of marijuana. Furthermore, the nonmedical prescription stimulant users also used more hallucinogens (26.3% *vs.* 1.9%), amphetamines (18.6% *vs.* 0.6%), anxiety medication (34.5% *vs.* 6.1%), ecstasy (17.8% *vs.* 1.0%) and pain medication (34.3% *vs.* 12.8%) (Hartung *et al.,* 2013:836).

Research identified several other factors associated with the nonmedical use of methylphenidate and similar drugs (Table 5-7), for example financial stress, religion, depression, cigarette use, perceived peer engagement in nonmedical use, field of study, sensation seeking[8], college enrolment, young adults, older students, less negative perceptions of nonmedical drug use and academic year. Studies have also identified risk factors that may be

[8] Sensation seeking is a personality trait that is defined as *“the need for varied, novel, and complex sensations and experiences and the willingness to take physical and social risks for the sake of such experiences”* (Zuckerman, 1979:10).

related to academic habits and performance such as skipping class, academic stress, procrastination, poor time management, worse subjective sleep quality, high parental expectations and weekly party behaviour. For example, according to the cohort study conducted by Arria, O' Grady, Caldeira and colleagues (2008:1054), nonmedical users study less (17.2 hours per week), socialise more (29.4 hours per week) and skipped class more often per week (16%) compared to non-users (19.7 hours per week, 24.8 hours per week, and 9.4% respectively). Since nonmedical users seem to be associated with bad academic habits, it has been postulated that these students use prescription stimulants to offset a partying lifestyle, instead of the idea that prescription stimulants are used to gain an academic edge (Arria, O' Grady, Caldeira, *et al.,* 2008:1056).

Research has additionally uncovered an association between nonmedical use of methylphenidate and related drugs and ADHD symptoms (Peterkin *et al.,* 2011:266; Poulin, 2007:749; Rabiner *et al.,* 2009b:268; Rabiner *et al.,* 2010:646; Singh *et al.,* 2014; Van Eck *et al.,* 2012:945). These researchers subsequently proposed that self-treatment of undiagnosed ADHD may be an underlying cause for the nonmedical use of these drugs. However, other academics have proposed that nonmedical use of stimulants may be an extension of the general propensity of individuals with ADHD for substance misuse (Benson *et al.,* 2015:64). According to a cross-sectional study that made use of the validated World Health Organization (WHO) Adult ADHD Self-Report Scale (ASRS), 71% of ADHD drug misusers have ADHD symptoms (Peterkin *et al.,* 2011:266). However another cross-sectional study that also used the ASRS declared a mere 17% of a group of persistent nonmedical users of prescription stimulants met "clinical criteria" for ADHD, indicating that many other factors play a role in persistent nonmedical drug use (Arria *et al.,* 2011:353). Arria and associates (2011:353) did make it clear that without comprehensive clinical evaluations it is impossible to know if these students really do have ADHD or whether the attention problems are a result of other issues that are associated with nonmedical users (such as illicit drug use). This limitation is especially noteworthy as there is convincing evidence to suggest that self-reported questionnaires are inefficient at differentiating between true ADHD and feigned ADHD symptoms (Mussa & Gouvier, 2014:198). Furthermore, students are aware of treatments for ADHD and so it can be argued that obtaining stimulants by going to a physician and getting a proper diagnosis and prescription is an easier and less expensive manner of obtaining stimulants than doing so illicitly (White *et al.*, 2006:265)

#### 2.2.1.3 Reasons for nonmedical use of methylphenidate and similar drugs

All the studies reviewed in the meta-analysis by Benson and affiliates (2015:62) that reported the reason for nonmedical use agreed that prescription stimulants are used mainly for academic

reasons. Although the studies described the reasons differently, the following the primary reasons for nonmedical use:

- To enhance academic performance (Clegg-Kraynok *et al.,* 2011:600; DuPont *et al.,* 2008:169; Emanuel *et al.,* 2013:1031; Garnier-Dykstra *et al.,* 2012:230; Lord *et al.,* 2009:524; Mache *et al.,* 2012:265; Micoulaud-Franchi *et al.,* 2014:1876; Peterkin *et al.,* 2011:266; Rozenbroek & Rothstein, 2011:361; Silveira *et al.,* 2014:104; Stock *et al.,* 2013:495; Teter *et al.,* 2006:1505; Tuttle *et al.,* 2010:221; Weyandt *et al.,* 2009:289).
- To improve concentration (Clegg-Kraynok *et al.,* 2011:600; DeSantis *et al.,* 2008:318; Emanuel *et al.,* 2013:1031; Gallucci *et al.,* 2014:184; Lord *et al.,* 2009:524; Mache *et al.,* 2012;265; McNiel *et al.,* 2011:370; Micoulaud-Franchi *et al.,* 2014:1876; Rabiner *et al.,* 2009b:264; Silveira *et al.,* 2014:104; Stock *et al.,* 2013:495; Teter *et al.,* 2005:256; Teter *et al.,* 2006:1505; Volger *et al.,* 2014:161; White *et al.,* 2006:265).
- To increase alertness (Clegg-Kraynok *et al.,* 2011:600; Emanuel *et al.,* 2013:1031; Lord *et al.,* 2009:524; Mache *et al.,* 2012:265; Teter *et al.,* 2005:256; Teter *et al.,* 2006:1505).
- To stay awake to study longer (DeSantis *et al.,* 2008:318; Emanuel *et al.,* 2013:1031; Lord *et al.,* 2009:524; Stock *et al.,* 2013:495).
- To help memorise (DeSantis *et al.,* 2008:318; Mache *et al.,* 2012:265).
- To be more efficient on academic assignments (Low & Gendaszek, 2002:285).

Besides academic reasons, recreational use is also prevalent in the literature as a reason for nonmedical use of these substances (Clegg-Kraynok *et al.,* 2011:600; DeSantis *et al.,* 2008:318; Emanuel *et al.,* 2013:1031; Garnier-Dykstra *et al.,* 2012:230; Lord *et al.,* 2009:524; McNiel *et al.,* 2011:370; Peralta & Steele, 2010:883; Rabiner *et al.,* 2009b:264; Stock *et al.,* 2013:495; Teter *et al.,* 2005:256; Teter *et al.,* 2006:1505; Volger *et al.,* 2014:161). Reasons forming part of recreational use include using these drugs to get high, to party and to delay the intoxicating effects of alcohol.

Research shows that the prevalence of nonmedical use for the intention of getting high is between 0% and 43% (Clegg-Kraynok *et al.,* 2011:600; DeSantis *et al.,* 2008:318; Emanuel *et al.,* 2013:1031; Gallucci *et al.,* 2014:184; Garnier-Dykstra *et al.,* 2012:230; Lord *et al.,* 2009:524; Silveira *et al.,* 2014:104; Teter *et al.,* 2005:256; Teter *et al.,* 2006:1505). “To party” or “to have fun” is reported between 5.7% and 65.2% of the time (DeSantis *et al.,* 2008:318; Garnier-Dykstra *et al.,* 2012:230; Lord *et al.,* 2009:524; Mache *et al.,* 2012:265; Rozenbroek & Rothstein, 2011:361; Silveira *et al.,* 2014:104; White *et al.,* 2006:265). Only three studies (Benham *et al.,* 2006:198; Gallucci *et al.,* 2014:184; Rabiner *et al.,* 2009b:264) commented on the use of prescription stimulants to prolong the effect of alcohol or other drugs; however, the only investigators that reported a prevalence rate reported that 1.5% of nonmedical users who

do not have a prescription for the drugs primarily use prescription stimulants for this reason (Gallucci *et al.,* 2014:184).

Another common reason, with prevalence rates between 1% and 31.4%, for the nonmedical use of methylphenidate and related drugs is for curiosity, experimentation or to try a novel experience (Clegg-Kraynok *et al.,* 2011:600; Emanuel *et al.,* 2013:1031; Garnier-Dykstra *et al.,* 2012:230; Lord *et al.,* 2009:524; Mache *et al.,* 2012:265; Micoulaud-Franchi *et al.,* 2014:1876; Peterkin *et al.,* 2011:266; Rozenbroek & Rothstein, 2011:361; Silveira *et al.,* 2014:104; Teter *et al.,* 2006:1505). Interestingly, results from a cohort study reveal that the prevalence of curiosity as a reason for nonmedical drug use waned from 18.9% in first year students to 1.3% by their fourth year of study; suggesting that the drug use may evolve from novelty seeking to the pursuit of improved academic performance (Garnier-Dykstra *et al.,* 2012:230).

Weight loss has also been reported as a reason for nonmedical use. This prevalence purportedly varies from 0% to 11.7% (DeSantis *et al.,* 2008:318; Emanuel *et al.,* 2013:1031; Gallucci *et al.,* 2014:184; Jeffers & Benotsch, 2014:415; Jeffers *et al.,* 2013:12; Lord *et al.,* 2009:524; Silveira *et al.,* 2014:104; Teter *et al.,* 2006:1505). Another reason given is “to counteract the effects of other drugs” (prevalence rates: 2.5% to 8%) (Clegg-Kraynok *et al.,* 2011:600; Emanuel *et al.,* 2013:1031; Teter *et al.,* 2005:256; Teter *et al.,* 2006:1505). Other miscellaneous reasons for endorsement has been reported to be: “social reasons”, “relaxation”, “getting things accomplished around the house”, “better concentration and alertness for long drives”, “confidence”, “increased enthusiasm”, “increased energy/activity level”, “decreased activity level”, “feeling less apathetic”, “maintain a habit”, “to treat self-diagnosed ADHD”, “to exercise better”, “to prevent other students from having an academic edge over me”, “manage pressure to succeed”, “stress reduction”, “help me manage my sleeping habits”, “because it’s safer than street drugs”, “I ran out of my own prescription” and “peer pressure” (Clegg-Kraynok *et al.,* 2011:600; DeSantis *et al.,* 2008:318; Emanuel *et al.,* 2013:1031; Gallucci *et al.,* 2014:184; Lord *et al.,* 2009:524; Low & Gendaszek, 2002:285; Mache *et al.,* 2012:265; Peterkin *et al.,* 2011:266; Rabiner *et al.,* 2009b:264; Rozenbroek & Rothstein, 2011:361; Teter *et al.,* 2006:1505; Volger *et al.,* 2014:161).

Research has also been done on reasons why students don’t use these drugs non-medically. Results from the College Life Study indicated that by their fourth year of study, 61.8% of students had been offered use of prescription stimulants at least once, but only between 34% and 42% had done so (Garnier-Dykstra *et al.,* 2012:229), begging the question as to why some students abstain from using these drugs. One study reports that as many as 74% of students who were interested in using methylphenidate non-medically did not use it because of a lack of availability. It seems that students who were not interested in using prescription cognitive enhancers were motivated by moral considerations (Singh *et al.*, 2014). Another study found

that the main reason why non-users refrain from nonmedical prescription stimulant use is the belief that it would cause mental or physical harm (Brandt *et al.,* 2014:275). The results of Arria, Caldeira, Vincent, and co-workers (2008:198) agree with both these reasons, showing that low perceived harm and high sensation seeking significantly and independently predict nonmedical stimulant use. Interestingly, other researchers discovered that perceived negative consequences from nonmedical prescription stimulant use is a deterrent only if those consequences are perceived as seriously severe (Lookatch *et al.,* 2012:90).

#### 2.2.1.4 Nonmedical use behaviour

2.2.1.4.1 Frequency of nonmedical use of methylphenidate and similar drugs by students

Relatively few studies have measured how often nonmedical users use methylphenidate, prescription stimulants, ADHD medications or cognitive enhancers. The studies that have looked at it wildly disagree on the frequency at which the drugs are used. While one study (Silveira *et al.,* 2014:104) reports most nonmedical users (46%) only use methylphenidate once a year, another (DuPont *et al.,* 2008:168) reports that most nonmedical users (45%) use it between 2 and 10 times per year. Two other studies coincide by reporting that half of nonmedical methylphenidate users use the drug at least once per month (Mache *et al.,* 2012:266; Maier *et al.,* 2013). In the studies that considered prescription stimulants, ADHD drugs and cognitive enhancers as groups, the frequency of use for most students in the study populations vary from as infrequently as 2-5 times in their lives, to as regular as 10-12 times in the past month (Arria, Caldeira, O'Grady, Vincent, Johnson, *et al.*, 2008:162; Bavarian *et al.,* 2013:669; Emanuel *et al.,* 2013:1030; McNiel *et al.,* 2011:371; Micoulaud-Franchi *et al.,* 2014:1876; Ott & Biller-Andorno, 2014; Stock *et al.,* 2013:495; Tuttle *et al.,* 2010:221; Underhill & Langdon, 2013:13; White *et al.,* 2006:264). For example, whereas Tuttle and affiliates (2010:221) state that 45% of the nonmedical users in their sample had only used prescription stimulants between two and five times in their lifetime, results from a different investigation (Bavarian *et al.,* 2013:669) show that more than 86% of students used prescription stimulants between one and nine times per academic term. Yet another study proclaims 85% of students use prescriptions stimulants on an average of three times per month or less (Stock *et al.,* 2013:495). The nonmedical use of these drugs may peak during stressful academic times, such as examinations (DeSantis *et al.,* 2008:321; Moore *et al.,* 2014:991; Van Hal *et al.,* 2013:112). In an investigation of longitudinal self-reported use of methylphenidate and amphetamine in conjunction with an analysis of the metabolites of these drugs in wastewater, the authors noted a significant increase in use of both of these substances during times of academic stress (Moore *et al.,* 2014:991). It can therefore be concluded that although it is difficult to come to a precise estimate, it appears as if students engage in nonmedical drug use relatively infrequently; however, this frequency may increase during stressful academic times.

2.2.1.4.2 Routes of administration of methylphenidate and similar drugs

Although most nonmedical users apparently use methylphenidate, prescription stimulants, or ADHD medications[9] orally, a small but consistent proportion of students use these drugs via other routes as well. It has been suggested that oral routes are preferred by nonmedical users who use the drugs for academic reasons while non-oral routes are preferred for recreational purposes (Barrett *et al.,* 2005:459). After oral administration, intranasal is the most common route of administration. Approximately 3.7% to 50% of students who use methylphenidate in a nonmedical manner snort the medication (Arria, Caldeira, O'Grady, Vincent, Johnson, *et al.*, 2008:163; Barrett *et al.,* 2005:459; DuPont *et al.,* 2008:170; Habibzadeh *et al.,* 2011:73). These rates correspond with those for prescription stimulants and ADHD drugs: 5-40.3% of students administer these drugs intranasally (Arria, Caldeira, O'Grady, Vincent, Johnson, *et al.*, 2008:163; Bavarian *et al.,* 2013:669; Brandt *et al.,*2014:274; Clegg-Kraynok *et al.,* 2011:600; Garnier-Dykstra *et al.,* 2012:230; Hall *et al.,* 2005:172; Hartung *et al.,* 2013:835; Herman *et al.,* 2011:20; McCabe & Teter, 2007:72; McNiel *et al.,* 2011:371; Rabiner *et al.,* 2009a:148; Teter *et al.,* 2006:1505; Weyandt *et al.* 2009:294; White *et al.,* 2006:264). Injecting crushed tablets is an uncommon reported route of administration of methylphenidate (Barrett *et al.,* 2005:459; Habibzadeh *et al.,* 2011:73) and prescription stimulants (Rabiner 2009a:148; Teter *et al.,* 2006:1505) among nonmedical users. There have also been reports of students smoking methylphenidate and other prescription stimulants (Barrett *et al.,* 2005:459; Bavarian *et al.,* 2013:667; McCabe & Teter, 2007:72; Teter *et al.,* 2006:1505; Weyandt *et al.,* 2009:294). Using these substances via non-oral routes of administration has been positively associated with both depressed mood (Teter *et al.,* 2010:295) and drug-related problems (McCabe & Teter, 2007:73). For example, the odds of experiencing drug-related problems are nine times, and 18 times greater if a nonmedical user reports intranasal administration or intravenous administration, respectively (McCabe & Teter, 2007:73).

As mentioned previously in paragraph 2.1.6, the type of formulation likely plays a role in the route of administration used. According to Arria, Caldeira, O'Grady, Vincent, Johnson, *et al.* (2008:163), while 17.3% of the nonmedical users in their sample snorted methylphenidate, only 3.8% used extended release products via intranasal administration.

[9] None of the studies that considered cognitive enhancers measured the route of administration used.

## 2.3 Knowledge of methylphenidate

Very few studies have evaluated how many students know of methylphenidate and what those students know. One study reports that while only 5.8% of the sample had used methylphenidate, more than 80% knew of it; however, the authors did not measure what they knew about it (Singh *et al.,* 2014). Another study reported that the most knowledgeable students are pharmacy students, then medical students. Again this study did not measure knowledge *per se,* instead the researchers measured whether or not the participants could identify prescription stimulants as cognitive enhancers or not (Franke *et al.,* 2011:61); in light of the heated debate regarding this subject, this may instead be considered a perception rather than knowledge.

Three studies could be found that investigated how much students know about methylphenidate or prescription stimulants, but even then researchers do not always distinguish between perception and knowledge. For instance, in the study conducted by Carrol and colleagues (2006:483) the authors conclude nonmedical users are more knowledgeable about the effects of methylphenidate than non-users. This was determined based on the degree to which true (e.g. study longer) and false (e.g. build muscle) statements regarding the effects of methylphenidate was endorsed. Yet, some of the effects that were considered to be true (such as study better and remember more) are still the subject of heated debate (refer to paragraph 2.5.3) and so, with the absence of empirical evidence for these statements, they could be considered perceptions rather than facts. Similarly Habibzadeh *et al.* (2011:73) also made use of true or false questions, and reported that users know more about methylphenidate than non-users. Once more the true and false statements contained statements such as “methylphenidate decreases learning”, which is difficult to evaluate. Another statement read “methylphenidate has no characteristics of addictive drugs and users do not become dependent” and is also difficult to evaluate since it has been shown that addiction is rare in the therapeutic context, but it is certainly possible (especially when high doses are used; refer to paragraph 2.1.6). The third study concurs with the previous two in that it also concluded that nonmedical users are more knowledgeable than non-users. These researchers measured knowledge by investigating how many side effects the students could identify as being caused by excessive stimulant use (Judson & Langdon, 2009:101). Despite the differences in these studies, all seem to indicate that prescription stimulants, such as methylphenidate, are generally known to students and that users are better informed thereof than non-users.

## 2.4 Lawful control of methylphenidate and unlawful procurement

### 2.4.1 International regulation and South African laws relating to the control of methylphenidate

As a result of its high abuse potential, methylphenidate was one of the very first drugs to be classified internationally as a Schedule II substance under the 1971 Convention on Psychotropic Substances (United Nations Information Service, 1997). According to this agreement (United Nations, 1971), the manufacture, trade, possession and use of Schedule II substances must be limited to medical or scientific purposes. Parties (i.e. countries, such as South Africa) that subscribed to this agreement must require that the manufacturing, trade (import and export) and distribution of Schedule II substances are controlled or done under licence. This requirement includes controlling authorised persons and organisations, controlling the aforementioned licences and ensuring that security measures are put in place to prevent the theft or diversion of these substances from such premises. Thorough records must be kept by manufacturers, wholesalers and retail distributors with regard to the quantities manufactured and the quantities held in stock as well as details of the quantity, supplier, recipient and date in the case of acquisition and disposal. The United Nations agreement stipulates that these substances may only be dispensed to an individual for use with a medical prescription in compliance with sound medical practice. Furthermore it suggests that the number of refills and the duration of the validity of such a prescription must be limited. Parties may prohibit the import of a Schedule II substance, in which case other Parties must ensure that the substance is not imported to the country or region in question. Currently, methylphenidate is prohibited in Belize, Nigeria, Senegal, Thailand, Togo, Turkey and Yemen (INCB, 2014:235). Finally, the agreement requires the participating parties to furnish annual statistical reports (such as of quantities manufactured) to the International Narcotics Control Board (INCB).

Under South African law, methylphenidate is classified as a Schedule 6 substance (Rossiter, 2014:508), which is equivalent to international Schedule II status. In accordance with the regulations of the 1971 Convention on Psychotropic Substances (United Nations, 1971) and the Medicines and Related Substances Act 101 of 1965 (Act 101, 1965), manufacturers must have a permit in order to manufacture Schedule 6 substances and keep thorough records, and importers and exporters must have a permit to import/export Schedule 6 substances. Whenever theft or unusual loss of a Schedule 6 substance occurs, it must be reported to the South African Police Services and the office of the Registrar of Medicines. The destruction of large quantities of Schedule 6 medicine may only take place with the written authorisation of the Medicine Control Council (MCC) in the specified quantity (MCC, 2010:127).

In addition, the Medicines and Related Substances Act 101 of 1965 (Act 101, 1965) mandates that Schedule 6 substances may only be sold by a pharmacist, a pharmacist's intern or assistant under the personal supervision of a pharmacist, authorised manufacturers and wholesalers, and any other person who has been authorised to do so. A prescription for a Schedule 6 substance may not be repeated and is only valid for 30 days after being issued. The quantity prescribed may not exceed that needed for 30 days of use (Act 101, 1965). When such a substance is sold, it must be recorded in a register which is to be balanced four times per annum. Pharmacies are to keep Schedule 6 substances under lock and key at all times and the key must be in the possession of the responsible pharmacist (SAPC, 2010:178). It should be noted that besides pharmacies, licence holders and authorised healthcare workers who administer it in the course of their practice, the Act of 1965 implicitly states that nobody may possess Schedule 6 substances without a prescription from an authorised prescriber. Furthermore, the sale, manufacture and use of Schedule 6 substances for any purpose besides a medical purpose[10] are prohibited, unless a permit has been issued by the Director-General. Offences committed under this Act are punishable by a fine or imprisonment for no more than 10 years (Act 101, 1965).

### 2.4.2 Diversion: sources of methylphenidate for nonmedical use

Despite it being such a highly controlled substance, studies showed that methylphenidate is readily available for nonmedical use. When asked how easy it is to obtain prescription stimulants such as methylphenidate, the majority of students (50-85%) across studies agreed that it is either very easy or somewhat easy (DeSantis *et al.,* 2008:320; Sharp & Rosén, 2007:76; Weyandt *et al.,* 2009:289), although in one study 77% of students did not know and only 16% said prescription stimulants are easy to obtain (McNiel *et al.,* 2011:373). According to another study, 37% of male students and 29% of female students believe they could get prescription stimulants from their peers (Hall *et al.,* 2005:169). Numerous other investigations have confirmed the main source of these substances for nonmedical use is students' friends and acquaintances (Benham *et al.,* 2006:199; DuPont *et al.,* 2008:168; Emanuel *et al.,* 2013:1032; Ott & Biller-Andorno, 2014; Rozenbroek & Rothstein, 2011:362; Table 5-8).

Diversion is defined as *"any intentional act that results in transferring a drug product from lawful to unlawful distribution or possession"* (Smith *et al.,* 2013:2292). A series of cross-sectional studies has found that between 46.2-54.5% of college students with ADHD have been approached to give or sell their prescribed stimulants over the course of a year (McCabe *et al.,*

[10] Medical purpose is defined in section 17 paragraph b of the Medicines and Related Substances Act of 1965 as "*for the purposes of the treatment or prevention of a disease or some other definite curative or therapeutic purpose, but does not include the satisfaction or relief of a habit or craving for the substance used or for any other such substance*" (Act 101, 1965).

2014:1179), and another study found that 56% were approached over a period of six months (Rabiner *et al.,* 2009a:148). When asked if they had ever been approached for this reason in their life, 76.8% of students confirmed they had been approached (Gallucci, Martin & Usdan, 2015:156). Similar results have been reported for younger patients. In a study of 1 536 pupils in grades six to eleven, 46.4% of high school pupils and 13.1% of middle school pupils had been asked to divert their prescribed stimulants (McCabe *et al.,* 2004:1103). In fact, 23% to 58.9% of college students reported they have in fact given away or sold their prescription stimulants (Emanuel *et al.,* 2013:1030; Gallucci, Martin & Usdan, 2015:156; Rabiner *et al.,* 2009a:148; Sepúlveda *et al.,* 2011:555; Upadhyaya *et al.,* 2005:803). At the time of the study, approximately one third of the students who had ever diverted their medication had done so in the past month (Gallucci, Martin & Usdan, 2015:157). A study of adults with prescriptions for methylphenidate reveals that, of the 44% of the participants who had diverted their prescribed methylphenidate, most gave it away while a handful admitted to selling it (Darredeau *et al.,* 2007:531). Aldridge and associates (2011:630) estimated that one in every six adults with ADHD in the USA had diverted their medication in the past month. In another study, 26% of adolescents in Canada admitted to giving away or selling the methylphenidate prescribed to them (Poulin, 2007:749).

Gallucci, Martin and Usdan (2015:157) investigated the main motivations for diversion and that found 75% of students gave their medication away in order to help another student during an academically stressful time. This finding ties in with the results of Checton and Greene (2011:268) who concluded that the most popular compliance gaining strategy used by non-prescription holders to get prescription stimulants is rationality, i.e. offering justifications for why they want to be given the medication. Notably, the next most common motivation (18%) was because the person receiving the medication had run out of their own medication (Gallucci, Martin & Usdan, 2015:157). Among those with a valid prescription, the most common primary motivation for selling their medication was “to make money” and the second most common was because they were offered money. It is curious how these students can have extra medication of such a highly scheduled substance in order to give it away or sell it. Results from a qualitative study indicate that some medical users may consume their prescription medication intermittently and give away or sell the surplus (DeSantis *et al.,* 2008:321). Interestingly, the most commonly noted risk factor for diverting prescribed ADHD medication is misusing one’s own medication (Darredeau *et al.,* 2007:531; Gallucci, Martin & Usdan, 2015:157; Poulin, 2001:1041; Rabiner *et al.,* 2009a:148; Sepúlveda *et al.,* 2011:555; Wilens *et al.,* 2006:412). In fact, according to one study, the risk of diversion is five times greater for a student with a history of nonmedical use compared to medical users without such a history (Gallucci, Martin & Usdan, 2015:157). These “diverters” are also more likely to be younger, to have received their prescription at a younger

age, to have used illicit substances (Darredeau *et al.,* 2007:531) and to have conduct disorder or substance abuse disorder (Wilens *et al.,* 2006:411).

The fact that nonmedical users get prescription stimulants from friends can explain why (as noted in paragraph 2.2.1.2) the risk of nonmedical use increases when a peer has a prescription for methylphenidate. It also supports the idea that nonmedical use increases proportionally to medical use (discussed in section 2.2.1) (Silveira *et al.,* 2014:105). Evidence for this link has been found in published results of the Student Drug Use Survey in the Atlantic Provinces, Canada done in 1998 (Poulin, 2001:1043) and 2002 (Poulin 2007:746). For instance, a class where at least one student reported giving or selling their prescription medication had a 1.52-fold increased risk ($p<0.001$) to also have nonmedical use by pupils with no prescription for the medication (Poulin 2007:746). Interestingly, researchers name lack of availability as the sole reason why interest in nonmedical use of cognitive enhancers does not convert into actual use, especially when it comes to stimulants (Singh *et al.,* 2014).

Several studies have noted that students most often obtain prescription stimulants for free (Advokat *et al.,* 2008:602; Arria, Caldeira, O'Grady, Vincent, Johnson, *et al.*, 2008:163; Clegg-Kraynok *et al.* 2011:600; DuPont *et al.,* 2008:168; Garnier-Dykstra *et al.,* 2012:232; Novak *et al.,* 2007; Silveira *et al.,* 2014:104). Albeit less common, nonmedical users are also reputed to buy these stimulants and even steal it (Table 5-8). When students do pay for the prescription stimulants, reported prices per pill vary between US $1 and US $4 (Advokat *et al.,* 2008:602), US $1 and US $10 (Arria, Caldeira, O'Grady, Vincent, Johnson, *et al.*, 2008:163) or US $3 and US $10 (DeSantis *et al.,* 2008:321), and a cohort study found the price to increase significantly over time (Garnier-Dykstra *et al.,* 2012:232). However, the fact that most users obtain the drugs for free might be an integral part of the problem with nonmedical use of these substances. Results from a study conducted by Sattler and co-workers (2014) reveal that high prices, compared to getting the drug for free, significantly reduced the participants' willingness to use drugs for cognitive enhancement.

After friends, the next most common source is usually family members, acquaintances or strangers, while other sources include obtained via the internet, one's own valid prescription[11], theft (including from a pharmacy), falsifying symptoms, black market, drug dealers and physicians (Table 5-8). In 2008, the National Centre on Addiction and Substance Abuse at Columbia University (CASA, 2008:7) managed to identify 159 websites that sell prescription drugs online. Eighty-five per cent of these websites did not require prescriptions and 43 of the sites specifically sold stimulants, of which methylphenidate was the most common. Despite this

[11] Those who named their "own prescription" as the source are students who have been prescribed the prescription stimulants for a valid indication and who then use it in a nonmedical manner.

fact, surprisingly few students make use of the internet to get a hold of the drugs. Most studies could not find any students who used this source and those studies that did found that, at most, only 5% used this source. ADHD patients have also reported being coerced into giving their medication away (Poulin, 2001:1041; Poulin, 2007:746; Weyandt *et al.,* 2009:289), hiding their medication to prevent it from being stolen (Weyandt *et al.,* 2009:289) and theft of their medication (Poulin, 2001:1041; Poulin, 2007:749; Rabiner *et al.,* 2009a:148).

What is concerning, however, is the emergence of reports (such as Clegg-Kraynok *et al.,* 2011:600; Novak *et al.,* 2007; Rozenbroek & Rothstein, 2011:361) of individuals who deceive physicians in order to get prescriptions for prescription stimulants like methylphenidate. Faking or exaggerating medical complaints for the purpose of receiving a reward (e.g. a prescription for prescription stimulants or academic accommodation) is known as malingering (Clemow & Walker*,* 2014:65). What is even more troubling is the conclusion of a review of 19 empirical investigations of malingered ADHD: students can feign ADHD symptoms so effectively that the majority of the most commonly used ADHD assessments have proven to be inadequate in distinguishing the deceivers from those with the disorder (Musso & Gouvier, 2014:197). It is unclear how common this practice is but one study reports that 44% of the participants knew a peer who had visited a physician to get a prescription for stimulant medication even though the peer did not believe he/she had ADHD (Carrol *et al.,* 2006:482). Furthermore, 19% of ADHD-diagnosed students declared that they have been asked how to fake ADHD symptoms (Advokat *et al.,* 2008:605). On the other hand, the only survey that could be found that measured physician perception of this matter revealed that less than 20% of physicians either agreed or strongly agreed that they are concerned about diversion when prescribing stimulants (Stockl *et al.,* 2003:418).

In summary, methylphenidate and similar stimulants most often slip out of their strict lawful control when those with prescriptions give them away or sell them. Strategies for minimising diversion should therefore focus on educating these individuals on the illegality of diversion, health risks of nonmedical use to their peers as well as ways to manage situations where they are asked to divert their medications (Gallucci, Martin & Usdan, 2015:157; Rabiner, 2013; Rostain, 2006:335). Furthermore, physicians should be vigilant when diagnosing ADHD and should make use of collateral information, such as parent reports, to support the diagnosis (Rostain, 2006:336).

### 2.5 The problem with nonmedical methylphenidate use

It has been established in previous sections that the nonmedical use of methylphenidate and similar drugs is a common occurrence among college students around the world, and that students mainly use these drugs with the intention of improving their academic performance.

Based on these findings, the question could be asked whether there is harm in students seeking to improve their academic performance. To determine the answer to this question, the potential risks and benefits must be weighed up. The main benefit might be the improvement in cognitive performance. Potential risks of nonmedical drug use include health considerations such as adverse reactions, drug interactions and associated risky drug use behaviours. Another potential risk is economic implications which include squandered resources because of diversion and overmedication, and resources spent to rectify overdoses, detoxification, withdrawal and drug dependence. Furthermore, consideration should be given to the moral perspectives of cognitive enhancement using pharmaceuticals. All these aspects will be considered in the subsequent section.

### 2.5.1 Health risks of nonmedical use of methylphenidate and similar drugs

The health risks associated with the nonmedical use of methylphenidate are multidimensional. Obvious health risks to all the parties involved are ADHD patients who divert their medication and thus who no longer receive the full benefit of their therapy, inappropriate and undue use of a scheduled drug, using superfluous doses to achieve greater effects, and using methylphenidate in conjunction with other drugs (Kaye & Drake, 2012:472; McCabe *et al.,* 2006b:53). When people engage in nonmedical drug use, they are placing themselves at risk of adverse health effects and even overdoses (Kaye & Drake, 2012:472). As established in section 2.1.5, nonmedical users were found to experience more side effects than medical users. It also appears as if nonmedical users do not heed the contra-indications of prescription stimulants. For example, an association has been found between experiencing anxiety and stress, and nonmedical prescription stimulant use despite the fact that prescription stimulants are contraindicated in anxiety (Dussault & Weyandt, 2013:94). Also, since the FDA has warned that the use of methylphenidate may cause sudden death if the patient has underlying cardiac abnormalities, the American Heart Association recommends that prescribers screen patients for cardiac abnormalities before prescribing stimulants such as methylphenidate, and monitor the patients accordingly (Vetter *et al.,* 2008:2416). When methylphenidate use is initiated by the individual, this screening and monitoring does not occur, meaning that nonmedical users are at increased risk of adverse cardiac events (Benson *et al.,* 2015:51).

Several studies (refer to Table 5-9) reported the simultaneous use of methylphenidate and similar drugs with other substances such as illicit drugs and alcohol. Methylphenidate is purportedly taken with alcohol, marijuana and cocaine by 14.2-63%, 2.8-53% and 0-21% of nonmedical methylphenidate users, respectively. The rates reported for prescription stimulants and ADHD drugs are strikingly similar (alcohol: 19.3-52.8%; marijuana: 17-47.1%; and cocaine: 0-19.8%). Reports (Table 5-9) showed that these drugs are also combined with illicit drugs such as gamma hydroxybutyrate (GHB), hallucinogens, heroin, inhalants, LSD, 3,4-

methylenedioxymethamphetamine (MDMA), psilocybin, and other prescription drugs like pain relievers, tranquilisers/sedatives, stimulants (amphetamines and ephedrine) and sleeping pills. It is important to highlight that it is not only the recreational nonmedical users who combine drugs; the nonmedical users who use methylphenidate and other prescription stimulants exclusively for academic reasons do this as well (Barrett *et al.,* 2005:459). In a letter to the editors of the Journal of Clinical Psychopharmacology, Barrett and Pihl (2002) remarked that users reported on combining alcohol and methylphenidate results because of their perception that it improved euphoria and reduced drunkenness. Four of the cases even compared the experience to the feeling caused by using low-grade cocaine with alcohol. There are also other, more substantial reports of students purposefully combining alcohol and prescription stimulants use to prolong the intoxicating effects of alcohol (Benham *et al.,* 2006:198; Gallucci *et al.,* 2014:184; Rabiner *et al.,* 2009b:264).

Little is known about the consequences of combining prescription stimulants such as methylphenidate with alcohol or other substances. In 1999, Markowitz and colleagues (1999:365) discovered that a specific metabolite, ethylphenidate, is formed upon co-ingestion of methylphenidate and ethanol. The presence of ethanol causes enantioselective transesterification of *ℓ*-MPH to *ℓ*-ethylphenidate by carboxylesterase 1 (CES1). This same enzyme is responsible for the de-esterification of methylphenidate to ritalinic acid (Patrick *et al.,* 2007). Therefore, the competitive inhibition of *ℓ*-ethylphenidate on *d*-methylphenidate hydrolysis increases the plasma concentration of *d*-methylphenidate. Subsequently, after the administration of racemic methylphenidate and ethanol, the absorption of *d*-methylphenidate is faster and exposure to it is prolonged. This not only heightens feelings of subjective positive effects but is also thought to increase the abuse potential of methylphenidate, which might explain the high incidence of methylphenidate-alcohol co-abuse (Patrick *et al.,* 2013:199). Barrett and co-workers (2006:258) found that students consume significantly more alcohol when it is co-ingested with methylphenidate. Concern has been raised that ethanol and stimulant co-ingestion may lead to excessive alcohol consumption or even poisoning since stimulants may counter the subjective depressant effects of alcohol (Novak *et al.,* 2007); however, there is little evidence to support this notion as it applies to methylphenidate.

A double-blind crossover study (N=16) conducted by Kollins and associates (2015:100) concluded that the cardiac adverse effects, specifically tachycardia, of co-ingested methylphenidate and delta-9-tetrahydocannibinol is additive. Furthermore there also seems to be additive and interacting subjective effects when these substances are combined. However, the extent and nature of the synergic abuse potential were unclear. There are similar concerns about combining cocaine and methylphenidate since cocaine also has stimulatory effects on the cardiac system (Boehrer *et al.,* 1992:92; Foltin *et al.,* 2003:152; Godfrey, 2009:197).

The nonmedical use of prescription drugs is not only associated with alcohol use and illicit drug use (refer to Table 5-7 and section 2.2.1.2), but has also been linked to high-risk sexual behaviours[12] (Benotsch *et al.,* 2011:154; Vidourek *et al.,* 2010:350), suicidal ideation (SAMHSA, 2014b; Vidourek *et al.,* 2010:348; Zullig & Divin, 2012:893), past year arrest (Wu *et al.,* 2007:199), both moderate and severe adverse alcohol-related consequences[13] (Egan *et al.,* 2013:76) and alcohol-related problems (Messina *et al.,* 2014:1801). According to Teter *et al.* (2003:216), while illicit methylphenidate use was significantly correlated with primary and secondary negative alcohol-related consequences, almost no difference was found between licit prescription stimulant users and non-users.

In summary, nonmedical stimulant use should not be considered an isolated behaviour to gain a competitive academic edge but rather as a part of a constellation of problematic behaviours (Arria & DuPont, 2010:425; McCabe *et al.,* 2005:103; McCabe *et al.,* 2006a:275; McCabe *et al.,* 2006b:45; McCabe *et al.,* 2009:68; Vidourek *et al.,* 2010:350), a phenomenon also known as "Jessor's Problem-Behaviour Theory" (Jessor, 1987:334). One group of researchers even postulated that students may not have a particular preference for methylphenidate, but instead use methylphenidate non-medically as a substitute for more expensive illicit drugs that are more difficult to obtain (Barrett *et al.,* 2005:459). This notion is supported by the results from the 2002-2009 National Survey on Drug Use and Health (NSDUH; N=443 041) that indicated that the nonmedical use of other prescription drugs, or even abuse of illicit drugs, precede nonmedical use of ADHD stimulants at least 77.6% of the time (Sweeney *et al.,* 2013:7).

Nonmedical users of stimulants such as methylphenidate are either unaware (Lookatch *et al.,* 2012:90; Weyandt *et al.,* 2009:293) or unconcerned (Judson & Langdon, 2009:102; White *et al.,* 2006:265) of the potential dangers that might result from this behaviour. According to a study by DeSantis and associates (2008:317) none of the 175 misusers in their study consulted medical professionals, pharmaceutical guides or even internet sites before using stimulants for the first time. Instead, the students relied solely on hearsay. According to Weyandt *et al.* (2009:293) more than one in five students strongly believed occasional prescription stimulant use to be harmless. Together with favourable images of friends' use, low perceived vulnerability to health risks has been associated with students' willingness to engage in nonmedical stimulant use (Stock *et al.,* 2013:495). Experiencing or anticipating adverse effects does not deter nonmedical

[12] Examples of such behaviours are engaging in oral sex, having multiple sexual partners, engaging in sex after alcohol or drug, use and engaging in unprotected sex.

[13] Moderate adverse alcohol-related consequences refer to experiences such as getting drunk, doing something that was later regretted, missing a class, damaging property, being hurt or injured, hurting or injuring someone else, having a verbal argument, driving a car while under the influence of alcohol and performing poorly on a test or project. Severe adverse alcohol-related consequences are, for example, receiving a ticket for a DUI/DWI, being in an accident, getting into a physical fight, being a victim of a crime, having sex later regretted, being taken advantage of sexually and taking advantage of another sexually (Egan *et al.,* 2013:73).

use (Maher, 2008:674) unless those adverse effects are very severe (Lookatch *et al.,* 2012:90). According to Sattler *et al.* (2014) not even severe side effects significantly reduce willingness to use a drug for cognitive enhancement.

### 2.5.2 The cost of diversion

The cost of diversion is two-fold, the first being wasted pharmacy expenditure and the second being cost spent on misusers in emergency rooms (Clemow & Walker, 2014:76). Diversion is costly and, as such, it is of special interest to second and third party payers of ADHD medications. Few studies have attempted to measure the cost of diversion. One study has estimated that US $3 million are spent by private insurance companies on diverted methylphenidate per month, accounting for 4.3% of the total value spent on methylphenidate by these companies. According to Aldridge *et al.* (2011:630), 8.3% (US $2.1 million) of Ritalin® products that insurers pay for are diverted. Although these percentages are relatively small compared to the total spending on ADHD medications, it is noteworthy that it translates to a staggering estimated annual amount of US $83 million lost by insurers due to diversion in the USA alone (Aldridge *et al.,* 2011:630). Cost of diversion stretches further than only money lost from medicine given away or sold. Costs are also incurred when ADHD patients require additional mental health services due to under-treatment or for indirect consequences (such as substance abuse) of under-treatment. The argument can even be made that there are costs to society in general due to loss of productivity as a result of undertreated ADHD (Aldridge *et al.,* 2011:633).

In 2013, 461 000 people reported receiving treatment for stimulant use problems in the USA (SAMHSA, 2014a:90). In 2010 there were 15 585 cases of emergency room visits in the USA as a result of nonmedical use of ADHD drugs (SAMHSA, 2013a:3). Although the costs incurred by misusers in emergency healthcare have not been determined, these figures make it clear that the amount may be significant.

### 2.5.3 Effectiveness of methylphenidate for academic nonmedical use

Stimulants have been shown to reduce symptoms of inattentiveness, hyperactivity and impulsivity in ADHD-diagnosed adults (70% of the time) and children (70-80% of the time) (Advokat & Scheithauer, 2013). Extrapolating from that finding the assumption can be made that stimulants will improve academic performance. However, current evidence indicates otherwise. Regardless of the fact that academic reasons are the most commonly cited nonmedical methylphenidate uses, several researchers remark that the nonmedical use of methylphenidate and similar products is associated with poor academic performance and not

academic excellence (see paragraph 2.2.1.2). This section will present evidence for the efficacy of methylphenidate in healthy adults in order to explore this apparent paradox.

Despite the numerous reports stating most (70-95%) nonmedical users find ADHD medications (Advokat *et al.,* 2008:603; Peterkin *et al.,* 2011:266; Rabiner *et al.,* 2009b:265) or prescription stimulants (Emanuel *et al.,* 2013:1032; Volger *et al.,* 2014:164) to be effective at enhancing academic performance, most review studies agree that the empirical data comes up short; some studies even reported a detrimental effect on memory and attention in the healthy (Advokat & Scheithauer, 2013 [ADHD medications]; de Jongh *et al.,* 2008:764 [MPH]; Normann & Berger, 2008:112 [MPH]; Outram, 2010:200 [MPH]; Repantis *et al.,* 2010:204 [MPH]; Smith & Farah, 2011:734 [MPH and dextroamphetamine]). While a comprehensive systematic review of 46 articles and meta-analysis of 19 papers conducted by Repantis and associates (2010:202) found some evidence that may suggest a positive effect on memory after a single dose of methylphenidate, no evidence was found to support the idea that methylphenidate improves wakefulness, attention or mood in healthy volunteers. Moreover, methylphenidate did not significantly improve cognitive function nor reduce sleepiness after either single or repeated intake of the drug. Smith and Farah (2011:735) reported similar findings from their review and suggested that stimulants, such as methylphenidate, may have a positive effect on cognition but that this effect is too small to be detected by most studies. Similarly, results from another review indicate that methylphenidate may improve working memory and processing speed; however, the investigators concede that the effects are small (Linssen *et al.,* 2014:973).

It is possible that individual differences are the reason for the considerable disparity between published results. For example, the degree to which stimulants enhance cognition might be dependent on baseline cognitive ability, where those with a low-baseline capability benefit from the drug and those with a high baseline are disadvantaged by the drug, or specific genotypes (de Jongh *et al.,* 2008:768; Smith & Farah, 2011:735). Considering the aforementioned evidence (or rather, the lack thereof), it has been suggested that the subjective effects (Repantis *et al.,* 2010:204) or even the expectancy-related placebo effects (Looby & Earleywine, 2011:440; Mommaerts *et al.,* 2013:71) of methylphenidate drive its nonmedical use as opposed to objective improvement in academic performance.

While methylphenidate may reduce the symptoms of ADHD, results from a review conducted by Advokat and Scheithauer (2013) indicate that the reduction of these symptoms do not necessarily impact the patient's quality of life and may only produce slight, clinically unimpressive improvements in academic performance. Therefore, there is little evidence to indicate that the reduction of these symptoms equates to cognitive enhancement in ADHD patients. The reason for this paradox remains a mystery. Interestingly, while considering the potential of using drugs to enhance cognitive performance, de Jongh and co-workers

(2008:768) warn that there is already evidence to indicate that different brain regions display different dose-response curves. This means that a dose that would be beneficial to the functioning of a specific behaviour may have a null or even detrimental effect on another. Furthermore, based on preliminary evidence from human and animal studies, these authors propose that the following direct trade-offs could occur with cognitive enhancement: (1) an improvement in long-term memory[14] could cause debility of working memory[15]; (2) more robust (stable) long term memories can decrease the ability to modify those memories (flexibility); and (3) cognitive stability (relating to working memory) may only be increased by decreasing the flexibility to alter behaviour.

To conclude, there is little evidence that methylphenidate is a true cognitive enhancer. Even the authors of the most optimistic review (Linssen *et al.,* 2014:972) caution that in the context of everyday life, in the absence of a controlled environment and sensitive tests, the possible enhancing effects of methylphenidate might pale next to the benefits of adequate sleep and a good work-life balance. Moreover, considering the likely trade-offs that may be required to enhance specific functions, the notion of the magic bullet smart pill is flawed (Quednow, 2010:154). On the other hand, there is evidence supporting that cognitive performance can be increased with exercise, good nutrition, adequate amounts of sleep and stress management (Smith & Farah, 2011:736). Sleep, especially, plays a well-established role in memory consolidation[16] (Kandel *et al.,* 2014:177). Hence students will likely benefit much more from studying regularly and ahead of the time, and attending class regularly instead of using methylphenidate to allow them to stay awake all night to study shortly before a test (Advokat & Scheithauer, 2013; Arria, O' Grady, Caldeira, *et al.,* 2008:1054; Clemow & Walker, 2014:72).

### 2.5.4 Ethical perspectives of nonmedical methylphenidate use

This section examines whether or not it is ethically right to use a pharmaceutical drug, either in a nonmedical manner or as prescribed, for cognitive enhancement. This question has caused considerable ambivalence among medical practitioners, bioethics communities (Racine & Forlini, 2010:2) and students. Several studies have documented that students who use methylphenidate and related drugs in a nonmedical manner for cognitive enhancement are more likely to think it is morally acceptable, while non-users think it is not (Brandt *et al.,* 2014:274; Ott & Biller-Andorno, 2014; Singh *et al.,* 2014).

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[14] Long term memory refers to information that is retained over hours or even years (Gazzaniga *et al.,* 2009:313).

[15] Working memory has been conceptualised as the "blackboard of the mind" and is where information is stored and manipulated in the short term. This information can either be from current sensory input or can be drawn from long-term memory (Gazzaniga *et al.,* 2009:317).

[16] Consolidation is the process whereby short term memories are converted into long term memories (Kandel *et al.,* 2014:165).

Cognitive enhancement has been defined as the use of prescription medication to improve cognitive function (e.g. concentration or memory) in healthy individuals (Forlini & Racine, 2012:606; Lucke *et al.,* 2011:38). Arguments for cognitive enhancement stem from the idea that there is nothing wrong with improving oneself and that such practices should be encouraged and not scorned (Harris, 2009:1533; Greely *et al.,* 2008:703). In fact, Greely and colleagues (2008:705) even state that provided the drugs are sufficiently safe and effective, cognitive enhancers should be freely and legally available to anyone who wishes to use them. This argument seems reasonable; however, history has shown that safe drugs do not exist. At best, drugs have benefits that outweigh the risks (Ragan *et al.,* 2013:592).

Additionally, several issues have been raised against using methylphenidate for cognitive enhancement. The first issue, and most obvious according to Chatterjee (2009:1532), is that the proven benefits of methylphenidate in healthy individuals are marginal whereas the health risks are not. (Refer to section 2.5.1 for detail regarding the health risks and section 2.5.3 for evidence of the benefits.) Especially the abuse potential especially is often underappreciated in these ethical debates (Lucke *et al.,* 2011:40). Secondly, should it become common practice to use methylphenidate for cognitive enhancement, concern has been raised that it would lead to coercion. In other words, individuals would feel pressured to take the drug for fear of 'being left behind' (Chatterjee, 2004:971; Greenly *et al.,* 2008:703; Racine & Forlini, 2010:3; Verster & van Niekerk, 2012:910) or even be forced to take such drugs in certain professions, such as medicine or the military (Chatterjee, 2004:971; de Jongh *et al.,* 2008:771; Greenly *et al.,* 2008:703). Thirdly, gaining this competitive advantage would most likely be more prevalent among those with superior financial means and so it might worsen social inequities (Chatterjee, 2004:971; de Jongh *et al.,* 2008:771; Verster & van Niekerk, 2012:910). On that note, Verster and van Niekerk (2012:910) argue that even though technologies such as computers are not accessible in all areas in South Africa for education purposes, that is no reason to ban their use. However, Chatterjee (2009:1533) points out that *"acknowledging the existence of disturbing inequities does not justify blithely adding more"*. Chatterjee (2009:1533) also states that it should not automatically be assumed that having smarter people, who are not necessarily wiser, will be beneficial to society. Yet another dilemma is that using drugs to improve academic performance can be considered unfair or even cheating (Chatterjee, 2004:971; de Jongh *et al.,* 2008:771; Verster & van Niekerk, 2012:909). Duke University in the USA announced in September of 2011 that unauthorised use of prescription medication to improve academic performance is considered cheating according to the official university policy in addition to being a violation according to the university's drug policy (McLaughlin, 2011).

There are many things to consider when deciding whether or not cognitive enhancement is ethically right. When it comes to nonmedical use of methylphenidate, the practice remains illegal

(Ragan *et al.,* 2013:592) and dangerous, and it cannot be considered a benign behaviour considering the health risks and abuse potential as previously discussed in paragraph 2.5.1. However is not illegal for healthcare practitioners to prescribe methylphenidate for cognitive enhancement as an off-label use, and such users are likely to be screened and monitored for health risks. It should, however, be noted that it is not justifiable to prescribe a dangerous drug, with a proven potential for abuse, to a healthy individual, especially in the absence of evidence for its efficacy (Verster & van Niekerk, 2012:909). Therefore, until the benefits of methylphenidate use for cognitive enhancement in healthy individuals are proven to be tangible and its risk minimal, it can be said that the ethical debate is trivial.

## 2.6 Chapter summary

In this chapter methylphenidate was discussed with regard to its pharmacodynamic and pharmacokinetic properties, indications, adverse effects, abuse potential and contra-indications. Furthermore the epidemiology of the medical and nonmedical use of methylphenidate and related behaviours were described in detail. Consideration was also given to what students know about methylphenidate as well as legal regulation and diversion of methylphenidate. Finally problems with nonmedical methylphenidate use were identified and discussed. Consequently, the aims of the literature objectives are met. The following chapter related to the results of the empirical investigation.

# CHAPTER 3: RESULTS

The results of the study are aggregated into two manuscripts which were submitted for consideration for publication. The title of the first manuscript is “Appropriate and non-medical use of methylphenidate by South African university residence students: prevalence, reasons for use and adverse effects” and second is entitled “Students’ perception of the perceived availability and diversion of methylphenidate in a South African tertiary academic institution”. Knowledge of methylphenidate is discussed under the heading “Additional results”. The references that were cited in each of the articles can be found at the end of the respective article as well as in the complete reference list at the end of the dissertation.

## 3.1 Manuscript 1

The manuscript entitled “Appropriate and non-medical use of methylphenidate by South African university residence students: prevalence, reasons for use and adverse effects” was submitted to the journal *Health SA Gesondheid* (refer to Annexure B). The paper was written according to the specific guidelines of the *Health SA Gesondheid* journal, as was given at http://www.elsevier.com/journals/health-sa-gesondheid/1025-9848/guide-for-authors#92000 on the 18th of August 2015 and has been included in Annexure D.

# Appropriate and non-medical use of methylphenidate by South African university residence students: prevalence, reasons for use and adverse effects

**Authors:**

Jessica Dreyer[1], Johanita Burger[1], Irma Kotze[2], Sandra van Dyk[2] and Marike Cockeran[1]

Jessica Dreyer: jessica.dreyer29@gmail.com; Johanita Burger: Johanita.Burger@nwu.ac.za; Sandra van Dyk: Sandra.VanDyk@nwu.ac.za; Marike Cockeran: Marike.Cockeran@nwu.ac.za

**Affiliations**

[1]Medicine Usage in South Africa (MUSA), North-West University, Potchefstroom, South Africa.

[2]School of Pharmacy, North-West University, Potchefstroom, South Africa

**Address**

Private Bag x6001, North-West University, Potchefstroom Campus, Potchefstroom, South Africa, 2520

**Correspondence to:**

Burger, Johanita

Mailing address: Private Bag x6001, North-West University, Potchefstroom Campus, Potchefstroom, South Africa, 2520

Phone: +27 18 299 2285

Fax: +27 87 231 4105

E-mail address: Johanita.Burger@nwu.ac.za

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**ABSTRACT**

Methylphenidate, a prescription stimulant with a known potential for abuse, is allegedly used by university students to improve academic performance. Residence students are apparently especially susceptible to the misuse of methylphenidate. The purpose of this study was to determine the extent of appropriate and non-medical methylphenidate use among residence students from a South African tertiary academic institution. Reasons for use, doses consumed and side effects experienced were investigated. The study followed a quantitative cross-sectional design and used a structured questionnaire to gather data. Appropriate users were defined as students who have only used methylphenidate as prescribed, whereas non-medical users were defined as those using methylphenidate without a prescription, or using prescribed methylphenidate in a non-medical manner (e.g. in excessive doses). The results indicated that one in four residence students (N=328) have used methylphenidate at least once in their lives. Only 7.3% (n=24) were appropriate users, whereas 16.8% (n=55) were non-medical users. Half of the appropriate users have never been diagnosed with ADHD. All non-medical users used methylphenidate to study or concentrate; however, 21.6% and 10.8% have also utilised it to party and get high, respectively. The preferred product, especially by non-medical users, was extended release methylphenidate (72.7%). The most common side effects experienced were sleep difficulties (69.0%) and reduced appetite (67.1%). In conclusion, there is evidence to suggest that methylphenidate is being used in non-medical ways by South African residence students. More research is required to verify and evaluate the off-label prescribing of methylphenidate to help students study.

**Keywords:**

**Methylphenidate, student, medical use, side effect, reason, nonmedical use**

## 1. INTRODUCTION

Methylphenidate is a prescription stimulant that is registered in South Africa for use in ADHD (attention-deficit/hyperactivity disorder) and narcolepsy (Rossiter, 2014). Reports from around the world, however, have indicated that students use this drug in non-medical ways (Clegg-Kraynok, McBean, & Montgomery-Downs, 2011; Eslami *et al.,* 2014; Mache, Eickenhorst, Vitzthum, Klapp, & Groneberg, 2012; Maier, Liechti, Herzig, & Schaub, 2013; Mazanov, Dunn, Connor, & Fielding, 2013; Micoulaud-Franchi, MacGregor, & Fond*,* 2014; Silveira, Lejderman, Ferreira, & da Rocha*,* 2014; Singh, Bard, & Jackson*,* 2014). Non-medical use can refer to using methylphenidate without a prescription, as well as using excessive amounts of prescribed methylphenidate (Arria, Caldeira, O'Grady, Vincent, Johnson, & Wish*,* 2008). The non-medical use of prescription stimulants is more common than medical use (Arria *et al.,* 2008; McCabe,

Teter, & Boyd, 2006; Rozenbroek & Rothstein, 2011; Silveira *et al.,* 2014). Medical use and non-medical use of prescription stimulants are, however, not mutually exclusive behaviours. According to Maier and co-workers (2013), 33% of students who have been prescribed methylphenidate have also used it in non-medical ways (e.g. for recreational reasons). Appropriate use, can therefore be defined as the use of prescribed methylphenidate in accordance to instructions (Hartung *et al.,* 2013).

Methylphenidate is usually well tolerated under normal therapeutic conditions (Leonard, McCartan, White, & King*,* 2004). The most common adverse effects associated with methylphenidate are headache, irritability, stomach-ache, dry mouth, mood liability, nervousness, depression, weight-loss, tachycardia, palpitations and vertigo (Godfrey, 2009; Klein-Schwartz, 2002:220; Leonard *et al.,* 2004). Methylphenidate furthermore reduced appetite in 28% of cases (Spencer *et al.,* 2005), and caused insomnia in 19% to 41% of cases (Epstein, Patsopoulos, & Weiser*,* 2014). When used in non-medical ways, however, prevalence rates of adverse effects may be higher than 70% (Advokat, Guidry, & Martino*,* 2008; Rabiner, Anastopoulos, Costello, Hoyle, McCabe, & Swartzwelder*,* 2009a).

The lifetime prevalence of non-medical methylphenidate use varies between 2.2% and 23% (Clegg-Kraynok *et al.,* 2011; Eslami *et al.,* 2014; Mache *et al.,* 2012; Maier *et al.,* 2013; Mazanov *et al.,* 2013; Micoulaud-Franchi *et al.,* 2014; Silveira *et al.,* 2014; Singh *et al.,* 2014). The majority of non-medical methylphenidate users start using the drug whilst at university (Silveira *et al.,* 2014). A meta-analysis by Benson, Flory, Humphreys and Lee (2015) concluded that being male and belonging to a sorority/fraternity are additionally both strongly correlated with non-medical prescription stimulant use. The most common reasons for non-medical use reported by students included to study and to concentrate. Less common reasons are to get high, to prolong the intoxicating effects of alcohol or to lose weight (Benson *et al.,* 2015).

Considering the abuse potential of methylphenidate and the associated risk of its non-medical use, it is crucial to understand the drug use behaviours of students so that prevention strategies can be developed and implemented. Despite extensive research in various countries, published research relating to this matter is limited in South Africa. Anecdotal evidence suggests the methylphenidate may also be used non-medically by students studying at South African universities, but the extent thereof is unknown.

This study aimed to describe the prevalence of both appropriate and non-medical use of methylphenidate, to clarify the reasons for use and to determine what side effects students experienced.

## 2. METHOD

This study made use of a structured questionnaire and had a quantitative cross-sectional design. Data were collected during May 2015. The study was conducted according to the Declaration of Helsinki and ethical approval was obtained from the Health Research Ethics Committee of the North-West University (NWU-00146-14-A1; refer to Annexure G).

### 2.1. Population and sampling

Ten residences from the chosen tertiary academic institution were randomly selected (five sororities and five fraternities). Together these residences house approximately 2400 students. The researcher attended a weekly meeting at each of the residences to explain the study and ask for voluntary participation. No incentives were given for participation. After explaining the study, questionnaires and informed consent forms were distributed to the students. The students who chose to participate had several days to complete the questionnaires and informed consent forms, which were gathered in sealed boxes left in the possession of the residence matron. Written informed consent was obtained from all participants.

### 2.2. Measuring instrument

The structured questionnaire was adapted from the validated Behaviours, Expectancies, Attitudes and College Health Questionnaire (Bavarian, 2012). The questionnaire had 23 items with questions relating to demographic characteristics as well as methylphenidate use behaviour. Students were asked to indicate their age, sex, faculty in which they were enrolled for study and their year of study. Methylphenidate use was assessed with the questions “Have you ever used methylphenidate?” and “Have you used methylphenidate during your time at university?” Students were furthermore asked, “Has a healthcare practitioner ever officially diagnosed you with Attention-Deficit/Hyperactivity Disorder or Attention Deficit Disorder (ADHD or ADD)?” to which they could respond with “yes”, “no” or “I do not know”. Respondents were also asked whether methylphenidate had been prescribed to them.

Appropriate users were defined as those students who have had prescriptions for methylphenidate and have never used it in excess or for non-medical purposes. These students were further subdivided into ADHD users and off-label users, based on whether or not they have ever been diagnosed with ADHD. Non-medical use was defined as using methylphenidate without a prescription or using prescribed methylphenidate for non-medical reasons (such as partying) and/or using it in excess. There were two types of non-medical users identified: those who have used methylphenidate but have never had it prescribed (non-prescription holders) and those who have used prescribed methylphenidate for non-medical reasons and/or in

excess of what had been prescribed (medical misusers; as defined in the study conducted by Hartung *et al.,* 2013).

To determine why students use methylphenidate, they were given a list of reasons and asked to indicate how often they have used methylphenidate for each of the given reasons. They could reply using a likert scale (always, usually, sometimes, rarely, never). Students could also give additional reasons for use. Similarly the participants were given a list of known side effects of methylphenidate and asked how often, if ever, they had experienced the effects. Again students could add to the list if they found it insufficient. The students were also supplied with a list of all the trade products of methylphenidate available in South Africa, including the product strengths, and asked to indicate all the products they have used and how many tablets they would typically consume per day.

### 2.3. Data analysis

Data were captured using Microsoft Excel® and analysed using IBM SPSS Statistics 22. Associations between categorical variables were assessed using the Pearson's chi-square test ($\chi^2$). The strength of any significant association was evaluated with Cramer's *V*; where ~0.1 was a small effect-size, ~0.3 a medium effect-size and 0.5 or larger was a large effect-size. Statistical significance was considered at a two-sided α-level of 0.05 or less.

## 3. RESULTS AND FINDINGS

Of the estimated 2400 potential participants, 328 residence students participated in the study. It is unknown how many students attended each of the meetings when the questionnaires were handed out, and therefore the response rate is conservatively estimated to be 14%. The demographic characteristics of the sample are summarised in Table 1. The mean age of participants was 20.1±1.2 years (range 18-26). There were more female than male participants (56.9% *vs.* 43.1%). Most (49.1%) of the respondents were in their first year of study, 25.9% were in their second year of study and 25.0% were in their third year or higher. The Faculty of Health Sciences and of Economic and Management Sciences were the two most commonly identified faculties, accounting for 21.8% and 25.5% of the study population, respectively.

The prevalence of methylphenidate use in this study was 25.6% (n=84). Appropriate users accounted for 7.3% (n=24) of the population, and the proportion of non-medical users was more than double at 16.8% (n=55). The two subgroups of appropriate users (ADHD users: 4.3%; and off-label users: 3%) and the two subgroups of non-medical users (non-prescription holders: 9.5%; and medical misusers: 7.3%) were approximately evenly distributed.

Generally, more men than women used methylphenidate in both appropriate and non-medical ways. However, the findings could not conclude whether or not there were statistically significant associations between the type of methylphenidate user (medical/ non-medical) and age, gender, faculty or year of study (Table 1).

The vast majority of methylphenidate users only started using methylphenidate later in life: 2.3% started before primary school, 8% started during primary school, 47.1% started during high school and 42.5% first used methylphenidate whilst at university. There was a statistically significant difference between the age of initiation of non-medical users compared to appropriate users: 66.7% of the appropriate users started using methylphenidate during high school while 54.5% of the non-medical users first used it during university ($p$=0.049). Out of the non-medical users, the vast majority (74.2%) of the non-prescription holders first used methylphenidate at university, compared to 30.4% of the medical misusers who first used methylphenidate at this time ($p$=0.002). The percentage of students in each respective age group who started using methylphenidate whilst at university increased with age (18-19 years: 22%; 20-21 years: 55.3% and 22 years and older: 72.7%; $p$=0.01). There was no statistical difference between genders regarding the time of first methylphenidate use. The prevalence of methylphenidate use during students' time at university, regardless of the first incidence of use, was 79.8% for appropriate users and 78.2% for non-medical users.

Appropriate users used methylphenidate significantly more often than non-medical users. Of the appropriate users, 45.8% used it on a daily basis, compared to 11.3% of non-medical users who used it daily (p=0.001). Non-medical users often used methylphenidate before examinations (73.6%), semester tests (43.4%) and class tests (18.9%).

The most common reasons for methylphenidate use among the appropriate users were to study (100%), to improve concentration (90.9%) and ADHD (54.5%) (Table 1). The only other reason for use indicated by the appropriate users was to exercise better (5.6%). Four students with a diagnosis for ADHD reported that they have never or rarely used methylphenidate to treat this condition. Out of all the students with a prescription for methylphenidate, regardless of whether they were appropriate or non-medical users, 52.1% (n=25) said they have not been diagnosed with ADHD, 45.8% (n=22) had been and 2.1% (n=1) were unsure. Out of the entire population, 9.1% (n=28) reported that they have used methylphenidate for ADHD. The appropriate users of methylphenidate who have not been diagnosed with ADHD have only used it to study (100%) and improve concentration (90%). The non-medical users have used methylphenidate mostly to study and improve their concentration (100% and 98%, respectively), although 21.6% (n=8) have used it to party and 10.8% (n=4) to get high. Other reasons listed by non-medical methylphenidate users were to exercise better, to lose weight and peer pressure (Table 1). A number of non-medical methylphenidate users (n=3) also indicated the following reasons for

use: “to see if it works”, “to get up early to stay awake and concentrate e.g. 2 o’clock in the morning” and “once to stay awake”.

The most popular methylphenidate formulation was extended release: 60 students have used extended release methylphenidate formulations, 10 have used immediate release formulations and 5 have used both. More appropriate users have used extended release formulations (72.7%) than immediate release formulations (27.3%). Among the non-medical users, 92.1% of students have used extended release formulations and 7.9% have used immediate release formulations. Extended release formulations were therefore significantly more likely to have been used, especially by non-medical users ($p$=0.043; Cramer’s $V$=0.262). The average dose of immediate release methylphenidate used per day was 12 mg (SD=4.1) for all the users, 11.4 mg for appropriate users and 12.9 mg for non-medical users ($p$=0.552). The average dose for the extended release formulations was 39.2 mg for appropriate and 38.9 mg for non-medical users ($p$=0.954).

The majority of students administered methylphenidate orally. However, four students reported snorting it and one student reported injecting it. The most common side effects experienced include sleep difficulties, reduced appetite, headache and irritation (refer to Table 2). As many as one in every five methylphenidate users reported always experiencing sleep difficulties and reduced appetite when using methylphenidate. With the exception of irritation and nervousness, more non-medical users experienced each of the side effects; however, none achieved statistical significance (Table 3). Additional side effects reported by students included: “drink a lot of water”, “erection”, “nausea”, “suppresses personality”, “dry mouth” and “toothache”. On average, appropriate and non-medical users both experienced 3.6 different side effects at least once. One third of the appropriate users (n=8) have experienced between three and four side effects at least once and 34.5% of non-medical users (n=19) have experienced five or more side effects at least once. It could not be established whether or not there was a statistical correlation between the number of side effects experienced and the average dose consumed ($p$=0.657).

## 4. DISCUSSION

The results of this study showed that one in four students have used methylphenidate and that non-medical use was more than twice as common as appropriate use (non-medical to appropriate use ratio 2.3:1). This finding is similar to that of studies conducted in the United States of America where the ratio of non-medical use to appropriate use was calculated at 2.5:1 (McCabe *et al.,* 2006) and 5:1 (Arria *et al.,* 2008). The prevalence rates for non-medical use among students who have a prescription for methylphenidate (50%) are very similar to the 47% found by Gallucci, Usdan, Martin and Bolland (2014) among an undergraduate sample of 1020

students. Methylphenidate use in the current study was relatively current since approximately 80% of the users indicated that they have used methylphenidate whilst at university. In total, 20.6% of the residence students have used methylphenidate whilst at university, a rate that is very similar to that reported by Bavarian *et al.* (2014) who investigated the illicit use of prescription stimulants among 554 university students.

The majority of students started using methylphenidate while attending high school and university, which is in accordance with the results of Castle, Aubert, Verbrugge, Khalid and Epstein (2007) who concluded that older children and younger adults are more likely to use ADHD medications than younger children and older adults, respectively. The non-medical users generally started using methylphenidate whilst at university and the fraction of students who started using methylphenidate at this time increases with age.

In general, the appropriate users reported using methylphenidate to help them study and concentrate. This use may be considered as part of the treatment of ADHD; however, a surprising result was that half of the students who have been prescribed methylphenidate have never been diagnosed with ADHD. These students reported using methylphenidate for academic reasons but not for any of the two registered uses for methylphenidate. This finding may be an indication of off-label methylphenidate prescribing. The risk-benefit ratio of prescribing methylphenidate for an off-label use such as studying is questionable. For instance, although other research has shown that users who have not been diagnosed with ADHD believed ADHD medications improved academic performance (Advokat *et al.,* 2008; Peterkin, Crone, Sheridan, & Wise*,* 2011; Rabiner, Anastopoulos, Costello, Hoyle, McCabe, & Swartzwelder*,* 2009b), there is little empirical evidence to support this perception. In fact, some studies even report detrimental outcomes regarding memory (Advokat & Scheithauer, 2013; de Jongh, Bolt, Schermer, & Olivier*,* 2008; Normann & Berger, 2008; Outram, 2010; Repantis, Schlattmann, Laisney, & Heuser*,* 2010; Smith & Farah, 2011). More research is needed to evaluate the prescription of methylphenidate for studying in light of the absence of empirical evidence for efficacy and methylphenidate's known potential for abuse and health risks.

According to Spencer *et al.* (2006), extended release methylphenidate formulations lower the abuse liability of methylphenidate by causing a more gradual drug uptake and dopamine receptor occupation. However, the current study found that extended release methylphenidate formulations were the preferred choice, especially among non-medical users, showing that extended release formulations do not seem to be "abuse-resistant". Still, it should be taken into account that the sample size of the current study was relatively small. More research is therefore needed to determine the effect of formulation on non-medical drug use practices. The maximum daily dose for immediate release methylphenidate is typically 60 mg and that of extended release formulations is 72 mg (American Academy of Child and Adolescent

Psychiatry, 2007). The average doses used by the participants in this study were below these maximums.

Only 13.9% of all methylphenidate users in the current study have never experienced any side effects. The rates of side effects experienced by non-medical users were similar to that found in previous studies (Advokat *et al.,* 2008; Rabiner *et al.,* 2009a). Non-medical users generally experienced more side effects than appropriate users, but statistical analysis failed to find a significant association.

## 5. CONCLUSIONS, LIMITATIONS & RECOMMENDATIONS FOR FUTURE RESEARCH

The current study had several limitations worth mentioning. First of all, the sample sizes were relatively small, which made it difficult to detect significant associations. It also limits the generalisability of the results to other residence students and other tertiary academic institutions in South Africa. Secondly, the results relied on self-reported data which could be accurately verified. Finally, the study had a low response rate, which brings forth the possibility of nonresponse-bias.

Despite these limitations, the study managed to gather evidence for non-medical methylphenidate use among residence students from a South African tertiary academic institution. The current study is one of the first to report that a significant proportion of methylphenidate prescriptions are not to treat ADHD or narcolepsy, but instead it appears as if methylphenidate is being prescribed to help students study and concentrate as an off-label indication. This deduction is supported by the fact that all of the off-label users stated they have only used methylphenidate for the reason it was prescribed to them, and the only reasons they gave were to study and concentrate better. More research is needed to verify and clarify the emergence of this off-label prescribing practice for methylphenidate. Furthermore, if confirmed, this practice should be critically evaluated in terms of the established risks and benefits of methylphenidate. Arria and DuPont (2010) warn that non-medical stimulant use is not just an attempt to gain a competitive edge, but it may be a vain attempt to compensate for skipping class or partying. Non-medical prescription stimulant users are also more likely to be involved in several problematic behaviours involving alcohol and illicit drug use (McCabe, Boyd, & Teter, 2009; Vidourek, King, & Knopf, 2010). Students who use methylphenidate without a prescription are furthermore not screened for contra-indications (Benson *et al.,* 2015).

Considering the abuse potential and the health risks of unmonitored methylphenidate use, education programmes could be developed to teach students of the risks of non-medical methylphenidate use and of the illegality of the practice. According to The Medicines and Related Substances Act 101 of 1965, the penalties of using methylphenidate without a

prescription in South Africa can include a fine or imprisonment for 10 years (Act 101, 1965). Since most non-medical users use methylphenidate before tests and examinations, support programmes could focus on providing students with alternative support during such academically stressful times.

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**TABLES**

**Table 1: Characteristics of the sample and methylphenidate users, and reasons for use**

| | | | Methylphenidate users | | | | |
|---|---|---|---|---|---|---|---|
| | **Study population** | | **Medical users** | | **Non-medical users** | | ***p*** |
| | N | n (%) | N | n (%) | N | n (%) | |
| **Characteristics** | | | | | | | |
| Age | 323 | | 24 | | 54 | | 0.964 |
| 18-19 years | | 138 (42.7) | | 10 (41.7) | | 22 (40.7) | |
| 20-21 years | | 136 (42.1 ) | | 11 (45.8) | | 24 (44.4) | |
| 22 years and older | | 49 (15.2 ) | | 3 (12.5) | | 8 (14.8) | |
| Gender | 325 | | 24 | | 55 | | 0.857 |
| Male | | 140 (43.1) | | 13 (54.2) | | 31 (56.4) | |
| Female | | 185 (56.9) | | 11 (45.8 ) | | 24 (43.6) | |
| Year of study | 320 | | 24 | | 54 | | 0.720 |
| 1st | | 157 (49.1) | | 12 (50.0) | | 29 (53.7) | |
| 2nd | | 83 (25.9) | | 6 (25) | | 9 (16.7) | |
| 3rd and higher | | 80 (25.0) | | 6 (25.0) | | 16 (29.6) | |
| Faculty | 325 | | 24 | | 55 | | 0.318 |
| Health Science | | 71 (21.8) | | 6 (25.0) | | 10 (18.2) | |
| Economic and Management Sciences | | 83 (25.5) | | 8 (33.3) | | 12 (21.8) | |
| Other faculties | | 171 (52.6) | | 10 (41.7) | | 33 (60.0) | |

**Table 1: Characteristics of the sample and methylphenidate users, and reasons for use**

| | | | Methylphenidate users | | | | |
|---|---|---|---|---|---|---|---|
| | **Study population** | | **Medical users** | | **Non-medical users** | | ***p*** |
| | N | n (%) | N | n (%) | N | n (%) | |
| **Reasons for use** | | | | | | | |
| To study | 78 | 78 (100.0) | 21 | 21 (100.0) | 53 | 53 (100.0) | 0.242 |
| To improve concentration | 76 | 73 (96.1) | 22 | 20 (90.6) | 51 | 50 (98.0) | 0.177 |
| For my ADHD or ADD | 65 | 27 (41.5) | 22 | 12 (54.5) | 40 | 12 (30.0) | 0.093 |
| To party | 56 | 9 (16.1) | 18 | 0 (0.0) | 37 | 8 (21.6) | 0.336 |
| To exercise better | 55 | 4 (7.3) | 18 | 1 (5.6) | 36 | 3 (8.3) | 0.533 |
| Peer pressure | 55 | 4 (7.3) | 18 | 0 (0.0) | 36 | 4 (8.3) | 0.540 |
| To get high | 56 | 4 (7.1) | 18 | 0 (0.0) | 37 | 4 (10.8) | 0.552 |
| To lose weight | 56 | 4 (7.1) | 18 | 0 (0.0) | 33 | 5 (8.3) | 0.662 |

**Table 2: Frequency of side effects experienced by users**

| Adverse effect experienced | N | Always n (%) | Usually n (%) | Sometimes n (%) | Rarely n (%) | Never n (%) |
|---|---|---|---|---|---|---|
| Sleep difficulties | 84 | 16 (19.0) | 12 (14.3) | 17 (20.2) | 13 (15.5) | 26 (21.0) |
| Reduced appetite | 82 | 18 (22.0) | 19 (23.2) | 9 (11.0) | 9 (11.0) | 27 (32.9) |
| Headache | 83 | 4 (4.8) | 10 (8.4) | 12 (14.5) | 17 (20.5) | 43 (51.8) |
| Irritation | 80 | 5 (6.3) | 8 (10.0) | 15 (18.8) | 9 (11.3) | 43 (53.8) |
| Heart racing | 75 | 9 (12.0) | 10 (13.3) | 8 (10.7) | 5 (6.7) | 43 (57.3) |
| Nervousness | 76 | 8 (10.5) | 5 (6.6) | 7 (9.2) | 12 (15.8) | 44 (57.9) |
| Stomach ache | 76 | 0 (0.0) | 3 (3.9) | 5 (6.6) | 9 (11.8) | 59 (77.6) |
| Anger | 77 | 2 (2.6) | 1 (1.3) | 8 (10.4) | 9 (11.7) | 57 (74.0) |
| Dizziness | 76 | 4 (5.3) | 4 (5.3) | 8 (10.5) | 10 (13.2) | 50 (65.8) |

**Table 3: Type of adverse effects experienced due to methylphenidate use**

| Adverse effect experienced | All users | | Medical users | | Non-medical users | | *p* |
|---|---|---|---|---|---|---|---|
| | N | n (%) | N | n (%) | N | n (%) | |
| Sleep difficulties | 84 | 58 (69.0) | 23 | 14 (60.9) | 49 | 37 (75.5) | 0.467 |
| Reduced appetite | 82 | 55 (67.1) | 23 | 14 (60.9) | 46 | 33 (71.7) | 0.736 |
| Headache | 83 | 40 (48.2) | 23 | 10 (43.5) | 48 | 25 (52.1) | 0.605 |
| Irritation | 80 | 37 (46.3) | 23 | 13 (56.5) | 45 | 21 (46.7) | 0.850 |
| Heart racing | 75 | 32 (42.7) | 22 | 9 (40.9) | 43 | 21 (48.8) | 0.260 |
| Nervousness | 76 | 32 (42.1) | 22 | 10 (45.5) | 44 | 19 (43.2) | 0.996 |
| Dizziness | 76 | 26 (34.2) | 22 | 8 (36.4) | 43 | 16 (37.2) | 0.377 |
| Anger | 77 | 20 (26.0) | 23 | 6 (26.1) | 43 | 13 (30.2) | 0.542 |
| Stomach ache | 76 | 17 (22.4) | 22 | 3 (13.6) | 43 | 12 (27.9) | 0.362 |

## 3.2 Manuscript 2

The second manuscript was submitted to the *South African Medical Journal* (refer to Annexure C for proof of submission) and is entitled “Students’ perception of the perceived availability and diversion of methylphenidate in a South African tertiary academic institution”. This manuscript was written according to the spesifications of the *South African Medical Journal* as set out in the author guidelines (refer to Annexure E) on the 19th of September 2015 from http://www.samj.org.za/index.php/samj/about/submissions#authorGuidelines.

# Students' perception of the perceived availability and diversion of methylphenidate in a South African tertiary academic institution

**Jessica Dreyer[1], Johanita Burger[1], Irma Kotze[2], Sandra van Dyk[2] and Marike Cockeran[1]**

**Affiliations:**

[1]Medicine Usage in South Africa (MUSA), North-West University, Potchefstroom, South Africa.

[2]School of Pharmacy, North-West University, Potchefstroom, South Africa

**Qualifications**

Jessica Dreyer: BPharm

Johanita Burger: BPharm, MPharm, PhD

Irma Kotze: BPharm, MBA

Sandra van Dyk: BPharm, MSc, PhD

Marike Cockeran: MSc (Statistics)

**Contact details:**

Jessica Dreyer: jessica.dreyer29@gmail.com; Johanita Burger: Johanita.Burger@nwu.ac.za; Irma Kotze: Irma.Kotze@nwu.ac.za; Sandra van Dyk: Sandra.VanDyk@nwu.ac.za; Marike Cockeran: Marike.Cockeran@nwu.ac.za

**Address:**

Private Bag x6001, North-West University, Potchefstroom Campus, Potchefstroom, South Africa, 2520

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## ABSTRACT

**Background:** Despite being a highly controlled substance, reports have emerged that methylphenidate is allegedly freely available for non-medical use. Little research is available to clarify how South African students acquire methylphenidate for illicit use.

**Objectives:** To determine where residence students from a South African tertiary institution get methylphenidate for both appropriate and non-medical use, where they think they could get it and how easy they think it is to acquire.

**Methods:** A quantitative cross-sectional study was carried out at a South African tertiary academic institution. Data were collected by means of a structured questionnaire that accessed the self-reported opinions and experiences of residence students.

**Results:** There were 328 participants (response rate 13.7%).The mean age of the participants was 20.1 years and 56.4% of the sample was female. Although all the appropriate users have obtained methylphenidate legally, they have also obtained it illegally from their friends (30.8%) and family (7.7%). The most common source for non-medical users was their friends (77.3%). Non-medical users also acquired methylphenidate using fabricated prescriptions (10.7%) and by buying it from pharmacies without a prescription (14.3%). Users and non-users had similar perceptions of where they thought they could get methylphenidate, except that users were more likely to think they can get it from friends (67.1% *vs.* 46.7%).

**Conclusion:** The current study presents novel evidence for methylphenidate diversion by university students in South Africa. Considering the abuse potential of methylphenidate, the diversion should be further explored and programmes developed to improve the legal control of methylphenidate.

**Keywords:** methylphenidate, diversion, student, South Africa, perceived availability, questionnaire

## 1. INTRODUCTION

Methylphenidate is a prescription stimulant which is registered in South Africa for use in attention-deficit/hyperactivity disorder (ADHD) and narcolepsy [1]. As a result of its high potential for abuse, methylphenidate is classified internationally as a Schedule II substance under the 1971 Convention on Psychotropic Substances [2]. In South Africa it has been given the equivalent status of a schedule six drug [1].

Despite strict control over this drug, it seems to be readily available for non-medical use in various countries [3-6]. Studies have found that between 50% and 85% of students agreed that it is either very easy or somewhat easy to obtain prescription stimulants such as methylphenidate [7-8]. According to Barrett and associates [5], 77.8% of the students in their study obtained methylphenidate from a friend or acquaintance with a prescription. Another study likewise reported that 71.4% of students received it for free from friends [3]. Methylphenidate diversion (defined as transference of methylphenidate from lawful control into unlawful hands) [9] therefore seems to be commonplace. Diverting methylphenidate has several implications, such as patients not benefitting from their therapy [10] and requiring additional medical care as a result of complications from untreated ADHD [11]. Diversion also has cost implications. Aldridge and co-workers [11] estimated that private insurers in the United States of America (USA) spend USD ($) 3 million on diverted methylphenidate per month, adding up to USD ($) 83 million lost to methylphenidate diversion annually in the USA alone. In addition, non-medical users may

incur health risks in terms of side effects (especially when doses are escalated to reach a desired effect) and potential drug interactions [10].

Diversion research pertaining to methylphenidate is scarce in South Africa. To the best of our knowledge, this study provides one of the first insights into the sources used to obtain methylphenidate by students from a South African tertiary academic institution. Furthermore, few studies have considered where non-users think they could get methylphenidate. Such perceptions may potentially allude to where non-users would consider obtaining methylphenidate from upon first interest. In summary, this study set out to determine how residence students acquire methylphenidate, were they believe they could get it and how easy they think it is to obtain methylphenidate. As with previous similar studies [3,8,12-13] a quantitative cross-sectional study design was utilised. University students were targeted since they have been shown to be more at risk of nonmedical prescription stimulant use than their non-enrolled peers [14]. Additionally residence students were chosen since they are allegedly more at risk of nonmedical prescription stimulant use than other students [7-8,12].

## 2. METHODS

This quantitative cross-sectional study gathered data using a structured questionnaire. Ethical approval for the study was obtained from the Health Research Ethics Committee of the North-West University (ethics number NWU-00146-14-A1). The study was conducted according to the Declaration of Helsinki.

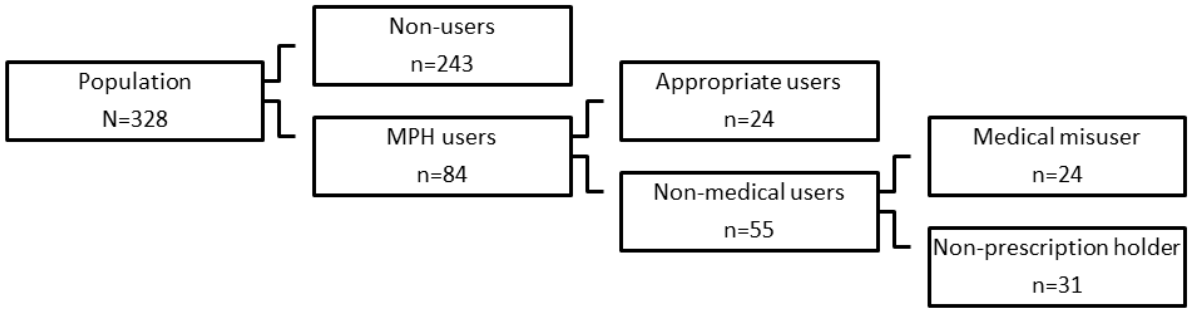
Data were collected during May 2015. Ten residences (five sororities and five fraternities) from a tertiary academic institution were randomly selected to partake in the study. The researcher attended weekly residence meetings at each of the residences to explain the study and ask for voluntary participation, after which the questionnaires and informed consent forms were distributed. All together the ten residences accommodated approximately 2400 students; however, it is unknown how many of these students attended the residence meetings at the time of data collection. The response rate was estimated to be 13.7%. Students were given several days to consider participation and complete the questionnaire. The students were not given any incentives for participation. Students could return the questionnaires and signed informed consent forms to sealed boxes left in the possession of the residence matron for four days.

### 2.2 The questionnaires and measures

The questionnaire had 23 items that related to demographic characteristics, methylphenidate use behaviours and perceptions, and knowledge of methylphenidate. The questionnaire was originally adapted from the previously validated Behaviours, Expectancies, Attitudes and College Health Questionnaire [6].

#### *2.2.1 Methylphenidate use and types of users*

The students were asked, “Have you ever used methylphenidate?” to which they could answer either “yes” or “no”. Students were given a list of all the trade names for this product in South Africa. Appropriate users were defined as those students who have a prescription for methylphenidate and have never used it in excess of what was prescribed or for non-medical reasons. Non-medical users were divided into two groups: non-prescription holders and medical misusers. The non-prescription holders were students who have used methylphenidate but have never had it prescribed. Medical misusers were students who have had methylphenidate prescribed but who have used it excessively, and/or for non-medical purposes. The breakdown of these groups is displayed in Figure 1.




Legend: MPH Methylphenidate

**Figure 1: Subgroup distribution**

*2.2.2 Sources and perceived available sources*

To determine from where the users obtained methylphenidate, the students were asked, "How often have you gotten your methylphenidate from (i) a pharmacy with a prescription written by a prescriber, (ii) a pharmacy with a fake prescription, (iii) a pharmacy without a prescription, (iv) friends, (v) family, and (vi) the internet?" For each of these options, the students could choose between likert-scale options (always, usually, sometimes, rarely, never). All students were also asked, "If you wanted to, do you think you could get methylphenidate from (i) a pharmacy with a prescription written by a prescriber, (ii) a pharmacy with a fake prescription, (iii) a pharmacy without a prescription, (iv) friends, (v) family, and (vi) the internet?" To this question, students were required to answer either "yes" or "no" to each of the six options. Participants had the opportunity to supply additional sources or perceived sources. Ease of acquisition was measured by asking how much they agree with the following two statements: "It is very easy to get hold of methylphenidate" and "It is easy to find a prescriber (e.g. doctor) to write a prescription for methylphenidate, even if a student does not really have ADD/ADHD". To assess whether or not the respondent knew that using methylphenidate without a prescription is illegal, they were asked the true or false question, "Using methylphenidate without a prescription is illegal", to which they could respond by choosing "true", "false" or "I don't know".

## 2.3 Data analysis

The data from the 328 participants were captured using Microsoft Excel® and analysed using IBM SPSS Statistics 22. Descriptive statistics included frequencies and percentages. The Pearson's chi-square test ($\chi^2$) was performed to determine the association between categorical variables. Cramer's *V*-value was calculated to assess the strength of this association, where ~0.1 was considered to be a small effect, ~0.3 a medium effect and >0.5 a large effect. Statistical significance was considered at a two-sided α level of 0.05 or less. Any missing values were excluded from the analysis.

## 3. RESULTS

The 328 participants were between the ages of 18 and 26 (mean 20.1 years; SD 1.2 years). Females accounted for 56.4% of the population. Most of the participants were in their first year of study (47%). The rest were in second (25.3%), third (14.9%), fourth (6.7%) and fifth year (2.7%); and eight students did not specify their year of study. Of all the students, 25.5% studied

under the faculty of economic and management sciences and 21.8% under the faculty of health sciences. The remaining students (52.6%) were from other faculties.

Of the 328 respondents, 84 (25.6%) had used methylphenidate at least once in their lifetime. These users were subdivided into appropriate users (n=24) and non-medical users (n=55). Of the non-medical users, 31 were non-prescription holders and 24 were medical misusers. The 84 users had obtained methylphenidate from a pharmacy with a valid prescription (70%), friends (58.8%), family (16.7%), a pharmacy using a fabricated prescription (8.0%), a pharmacy without a prescription (8.0%) and from the internet (4.1%). Only two students gave additional sources: one admitted to obtaining methylphenidate from an acquaintance and the other from a Facebook advert. All of the appropriate users indicated obtaining their methylphenidate using a valid prescription at a pharmacy (100%); however, some of them also admitted to obtaining methylphenidate from their friends (30.8%) and family (7.7%). Among non-medical users, the most commonly reported source of methylphenidate was friends (77.3%), a pharmacy with a prescription (54.5%) and family (22.6%). A small proportion of the non-medical users also got methylphenidate from a pharmacy without a prescription (14.3%), with a fake prescription (10.7%) and from the internet (3.7%). The only two statistically significant differences between the manner in which appropriate and non-medical users obtained methylphenidate were that appropriate users were more likely to have obtained the drug legally, *i.e.* from a pharmacy with a valid prescription (100% *vs.* 54.5%; $p$=0.03) and less likely to have obtained it from friends (30.8% *vs.* 77.3%; $p$=0.01). Likewise, when comparing the two types of non-medical users, medical misusers were statistically less likely to have received it from friends than the non-prescription holders (47.1% *vs.* 96.3%; $p$<0.0001).

All respondents were asked where they thought they could get methylphenidate if they wanted to. The results are shown in Table 1. Three students gave additional sources: two said they would get it from a physician and the third indicated asking a peer who uses methylphenidate where to get it. The only difference in perception between users and non-users was that it was more common for a methylphenidate user to think that they could get methylphenidate from friends ($p$<0.01) or family ($p$=0.04). Non-medical users more often thought that they could get methylphenidate from the internet ($p$=0.04) and less often from a pharmacy with a valid prescription ($p$<0.01) than appropriate users. Significantly fewer ($p$<0.01) non-prescription holders believed they could get methylphenidate from a pharmacy with a valid prescription than the medical misusers.

**Table 1: Perceived available sources for methylphenidate**

| Source | Population | | | | | Users | | | | | Non-medical users | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Users | | Non-users | | *p* | Appropriate users | | Non-medical users | | *p* | Non-prescription holders | | Appropriate misusers | | *p* |
| | N | n (%) | N | n (%) | | N | n (%) | N | n (%) | | N | n (%) | N | | |
| Pharmacy with a prescription | 81 | 65 (80.2) | 217 | 182 (83.9) | 0.460 | 24 | 24 (100.0) | 52 | 36 (69.2) | **0.002** | 28 | 15 (53.6) | 24 | 21 (87.5) | **0.008** |
| Pharmacy with a fabricated prescription | 70 | 13 (18.6) | 199 | 36 (18.1) | 0.929 | 20 | 2 (10.0) | 47 | 9 (19.1) | 0.355 | 26 | 5 (19.2) | 21 | 4 (19.0) | 0.987 |
| Pharmacy without a prescription | 70 | 7 (10.0) | 199 | 17 (8.5) | 0.713 | 20 | 1 (5.0) | 47 | 5 (10.6) | 0.460 | 26 | 2 (7.7) | 21 | 3 (14.3) | 0.466 |
| Friends | 76 | 51 (67.1) | 212 | 99 (46.7) | **0.002** | 22 | 12 (54.5) | 51 | 37 (72.5) | 0.133 | 29 | 23 (79.3) | 22 | 14 (63.6) | 0.214 |
| Family | 71 | 29 (40.8) | 205 | 57 (27.7) | **0.041** | 20 | 6 (30.0) | 48 | 22 (45.8) | 0.227 | 26 | 11 (42.3) | 22 | 11 (50.0) | 0.594 |
| Internet | 70 | 14 (20.0) | 199 | 60 (30.2) | 0.102 | 20 | 1 (5.0) | 48 | 13 (27.1) | **0.040** | 28 | 10 (35.7) | 20 | 3 (15.0) | 0.111 |

As shown in Table 1, 75.9% of the non-medical users agreed or strongly agreed that methylphenidate is easy to get hold of while only 33.3% of the appropriate users thought so. When asked the same question, almost half (46.6%) of the non-users replied they did not know and 37.3% of them either agreed or strongly agreed with the statement. The participants were also asked if they think it is easy to find a prescriber to write a prescription for a student, even if the students does not have ADHD, with which 50% of the appropriate users either disagreed or strongly disagreed. The answer to this question was evenly spread between the non-medical users, with 35.8% disagreeing or strongly disagreeing, 32.1% not knowing and 32.1% agreeing or strongly agreeing. The students who have never used methylphenidate mostly replied that they do not know (54.2%), with only 20.8% agreeing or strongly agreeing with the statement. Of note, one student added that "it depends; I study pharmacy: some of the doctors help you if you ask for it". Most users (73.8%) knew that it is illegal to use methylphenidate without a prescription, while only 63.0% of the non-users knew this ($p$=0.26). This knowledge was more common among appropriate users (79.2%) than non-medical users (70.9%; $p$=0.83). Further analysis showed that 80.8% of the students who have had methylphenidate prescribed knew use without a prescription is illegal while only 61.3% of the non-prescription holders knew it ($p$=0.16). Unfortunately, due to the limited sample size, it could not be determined whether any of these comparisons reached statistical significance.

**Table 2: Perceived ease of acquisition**

| | N | Disagree/ strongly disagree n (%) | I do not know n (%) | Agree/ strongly agree n (%) |
|---|---|---|---|---|
| "It is very easy to get hold of methylphenidate" | | | | |
| Population | | | | |
| Users | 83 | 24 (28.9) | 7 (8.4) | 52 (62.7) |
| Non-users | 236 | 38 (16.1) | 110 (46.6) | 88 (37.3) |
| Users | | | | |
| Appropriate users | 24 | 13 (54.2) | 3 (12.5) | 8 (33.3) |
| Non-medical users | 54 | 10 (18.5) | 3 (5.6) | 41 (75.9) |
| "It is easy to find a prescriber (e.g. doctor) to write a prescription for methylphenidate, even if a student does not really have ADD/ADHD" | | | | |
| Population | | | | |
| Users | 82 | 32 (39.0) | 28 (34.1) | 22 (26.8) |
| Non-users | 236 | 59 (25.0) | 128 (54.2) | 49 (20.8) |
| Users | | | | |
| Appropriate users | 24 | 12 (50.0) | 8 (33.3) | 4 (16.7) |
| Non-medical users | 53 | 19 (35.8) | 17 (32.1) | 17 (32.1) |

## 4. DISCUSSION

The study revealed that methylphenidate users make use of both legal and illegal sources to obtain methylphenidate. As can be expected, all of the appropriate users report having obtained methylphenidate from a pharmacy using a valid prescription; however, some of the students who use methylphenidate as prescribed have also obtained it illegally from friends and family members. Checton and Greene [15] conducted an investigation to determine why patients divert prescription stimulants. These researchers reported that 18% of the prescription holders gave their medication to a person whose own medication had run out. It is therefore possible that appropriate users in the current study got medication from their friends or family because their own medication had run out. Nevertheless, this action is still illegal and creates the problem that the friend or family member could not have enough medication for their own use (that is, if they had a prescription for methylphenidate in the first place).

The majority of the non-medical users (77.3%) reported getting methylphenidate from a friend and approximately one in five students of these students got it from a relative. This finding strongly agrees with the results of Barrett and colleagues [5], who reported that 77.8% of their non-medical users got methylphenidate from friends, and with the results of Silveira and associates [3], who found that 71.4% got it from friends or relatives. It is possible that these friends or relatives had prescriptions for methylphenidate since researchers have reported that students with ADHD are approached and asked to sell or give their medication away[12,16]. Gallucci and co-workers found that as many as 76.8% of students reported being asked to give away or sell their medication in their lifetime and that 58.9% of the students with prescriptions had done so[13].

The second most common source for the non-medical users was from a pharmacy with a valid prescription, although the rates measured in this study were nearly double of what were found in a previous study [3]. Similar to another study [17], very few students used the internet as a source. Unlike previous studies, the current study uncovered two sources that, to the best of our knowledge, have not been described in publications. A small but significant proportion of non-medical methylphenidate users acquired methylphenidate from a pharmacy with a fake prescription or even acquired it from a pharmacy without a prescription.

The strong similarity between where users think they may get methylphenidate and where non-users think they could get it is notable. It indicates that if the non-users would want to start using methylphenidate, they would likely look for it in the correct places. Interestingly, the only point on which users and non-users differed in their perceptions of perceived availability was regarding friends as a source. Peer engagement in non-medical prescription stimulant use has been identified as a risk factor for non-medical use [18]. Therefore it is likely that more users would think they can get methylphenidate from friends if more of their friends engaged in this activity as well. On the other hand, fewer non-medical users may believe they could get methylphenidate from their friends because fewer of their friends might actually be using methylphenidate. It is also notable that 83.9% of the non-users thought they could get a prescription for methylphenidate, but only 20.8% agreed or strongly agreed that it is easy to find a prescriber who would prescribe methylphenidate to a student without ADHD. It is possible that the students who thought they could get a prescription may believe they have ADHD; however, more research is needed to explain these conflicting perceptions.

Most non-medical methylphenidate users thought it is easy to get a hold of methylphenidate while most non-users did not know. This result may be very significant since one study found that the sole reason why interest in prescription stimulant use for cognitive enhancement did not convert into actual use is due to limited availability [4]. In other words, students who have easy

access to methylphenidate may be more tempted by non-medical use compared to students who do not know whether they could get it.

A relatively large proportion of students who have used methylphenidate but have never had it prescribed, and a large proportion of those who have never used methylphenidate did not know it is illegal to use methylphenidate without a prescription. This finding poses a potential area for intervention. Educating non-prescription holders about the illegality of their methylphenidate use may aid the effort to reduce this practice. Educating non-users may be just as important to prevent any interest in non-medical methylphenidate use from converting to actual use.

This study has several limitations that should be noted. First of all, although the exact response rate is impossible to determine, the estimated rate is low, which presents the possibility of reporting bias. Furthermore, the results are subject to the limitations associated with using self-reported reports. Thirdly, the study was conducted at a single tertiary academic institution in South Africa and only included residence students. This fact combined with the small sample size means that the results are not generalisable to the particular tertiary institution, all residence students or even all South African university students. Despite these limitations, the study is one of the first to report on methylphenidate diversion in South Africa and it managed to detect several meaningful results.

To conclude, there is evidence of methylphenidate diversion by students in the present study population. Students, both with prescriptions for methylphenidate and those without, should be educated about the dangers and illegality of non-medical methylphenidate use and diversion. Furthermore, more research is required to investigate methylphenidate diversion in South Africa so that programmes may be developed to improve its legal control.

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## 3.3 Additional results

All the results of the study have been described in either manuscript 1 or manuscript 2 besides the results pertaining to knowledge of methylphenidate. A knowledge score was calculated based on the students' replies to true or false statements where correct answers carried a weight of 2, incorrect answers a weigh of 0 and the reply "I don't know" a weight of 1. With regard to knowledge of methylphenidate, users scored a mean of 5.7 out of a maximum of 8. The knowledge score of the non-users was statistically lower (5.1; $p$=0.002), in agreement with those of similar studies (Habibzadeh *et al.,* 2011:73; Judson & Langdon, 2009:101). There was no statistically significant difference between nonmedical methylphenidate users and medical users.

## 3.4 Chapter summary

Chapter 3 expressed the results in the form of two manuscripts and an additional section; thereby fulfilling the empirical objectives of the study. Chapter 4 concludes the content of the dissertation with the final conclusions based on the study objectives, study limitations and strengths, and recommendations for future research.

# CHAPTER 4: CONCLUSIONS AND RECOMMENDATIONS

## 4.1 Conclusion

The following conclusions are derived from the objectives set forth for the literature and empirical phases of the study.

### 4.1.1 Literature objectives

The literature objectives were to:

(1) describe methylphenidate as a pharmacological entity with regard to its mechanism of action, adverse effects and drug interactions;
(2) describe the registered and off-label indications for the use of methylphenidate;
(3) determine the national and international prevalence and epidemiology of the use of methylphenidate, for medical and nonmedical reasons; and
(4) describe the legal aspects of the diversion of methylphenidate and methylphenidate use.

Methylphenidate is a Schedule 6 stimulant that is chemically related to amphetamine. Its mechanism of action involves the inhibition of DAT, which makes it an indirect dopamine agonist. Methylphenidate is registered for use in ADHD and narcolepsy, but may also be effective for other conditions such as cancer-related fatigue, Alzheimer's disease and Parkinson's disease. Adverse effects associated with methylphenidate include, among others, tachycardia, nervousness, insomnia and decreased appetite.

Despite abuse seeming rare under therapeutic conditions, methylphenidate has a high potential for abuse. The use of this drug has increased dramatically across the world for the last three decades. Furthermore, the nonmedical use of methylphenidate is a commonly documented occurrence in several countries, although such records pertaining to South Africa in particular are limited. Nonmedical use appears to be especially prevalent in hostel students. Nonmedical use is usually endorsed for academic purposes (such as studying for longer) but it is also used recreationally. Few studies have measured what students know of methylphenidate and those that have are difficult to compare. Despite being strictly controlled, methylphenidate is available to students for nonmedical use, usually from their peers. The ethical debate aside, this practice of nonmedical methylphenidate use can be considered a problematic behaviour in light of the associated health risks, economic costs and absence of empirically proven efficacy in cognitive improvement in healthy adults. Considering the lack of information on this topic in South Africa and the important implications of nonmedical drug use, it was shown that an investigation of the medical and nonmedical use by South African hostel students is warranted.

### 4.1.2 Empirical study objectives

The empirical objectives of the study were to:

(1) determine how many hostel students use methylphenidate;
(2) determine the relationship between demographic information and the use of methylphenidate;
(3) determine the relationship between the manner of methylphenidate use and the formulation of methylphenidate products;
(4) determine the initiation to and frequency of using methylphenidate;

(5) ascertain the reasons why hostel students use methylphenidate;
(6) determine the side effect profile the students experience when using the drug;
(7) identify sources of diversion and perceived availability of the drug;
(8) ascertain the differences in the students' knowledge with regard to the use of methylphenidate between non-users of methylphenidate and the user subgroups.

This study uncovered a significant proportion (84/328) of methylphenidate users among hostel students and furthermore found evidence of significant current use: the prevalence of use at university was nearly as high as the lifetime prevalence. There was no association between methylphenidate use and demographic characteristics such as gender or age, which coincides with other international studies (refer to Table 5-7).

Most students only started using methylphenidate whilst at high school or university, which concurs with results from prescription trends that reported ADHD medication use was more likely among older children and younger adults (Castle *et al.,* 2007:336). Medical users were more likely to use methylphenidate every day than nonmedical users. This finding supports the notion that nonmedical users turn to methylphenidate in times of academic stress (Moore *et al.,* 2014:991), instead of using this drug every day like medical users.

The most common reasons for use were academic while a handful of students used it for recreational reasons, a result that also coincided with the literature cited in paragraph 2.2.1.3. Out of the entire study population, 9.1% used methylphenidate for ADHD. Approximately half of the students who had been prescribed methylphenidate reported that they have never been diagnosed with ADHD. A likely conclusion is that these students were prescribed methylphenidate for an off-label use, possibly to help them study and concentrate.

Most methylphenidate users have experienced adverse effects from methylphenidate use. As in other studies (Advokat *et al.,* 2008:602; Rabiner *et al.,* 2009a:150), the most common adverse effects were sleep difficulties and reduced appetite. Although the prevalence rates of adverse

effects experienced were higher among the nonmedical users, it could not be determined whether the prevalence of adverse effects were associated with the type of user or not. The percentage of nonmedical users who experienced side effects were comparable to those from other studies (Advokat *et al.,* 2008:602; Rabiner *et al.,* 2009b:266). That said, the prevalence rates of adverse effects experienced by medical users were all, with the exception of headaches, higher than rates reported in a large randomised, double-blind, clinical trial (Spencer *et al.,* 2005:460). While it is possible that the rates of adverse events may differ in practice from that seen under the strictly controlled conditions of a clinical trial, comparability between these rates is hampered by the fact that the current study relied on self-reported data and had a small sample size. The route of administration was not analysed against the side effects experienced as very few participants used non-oral routes of administration. No correlation could be confirmed between the average dose consumed and the number of side effects experienced.

The average dose used for immediate release products was 12 mg and that of extended release products was 38.5 mg, both of which are well within the therapeutic parameter. The majority of methylphenidate users administered it orally. Given that very few students used other routes of administration, it was not feasible to analyse the route used in conjunction with the formulation type used.

A significant association could be found between the preferred formulation and the type of methylphenidate user. Contrary to the outcome one would expect based on the literature, all users, but especially the nonmedical users, most often used extended release methylphenidate products. It is possible that this association was driven by market popularity and thereby availability for nonmedical use instead of individual preference for the extended release products. It is furthermore possible that the popularity of the extended release products in this study was related to the few cases of non-oral administration seen in the sample, because extended release products are thought to be less effective for non-oral administration (refer to section 2.1.6). More research is required to explain this finding.

As found elsewhere in the world (Table 5-8), the most common source of methylphenidate for nonmedical use was from friends. Approximately a third of the medical users have also relied on these sources to acquire methylphenidate. Although only a fraction of the nonmedical users have used these sources, it is notable that students reported that they have been able to acquire methylphenidate from pharmacies with a fake prescription and from pharmacies without a prescription. Research should be conducted to confirm this finding and clarify how this occurs. The perceived sources that may be used to acquire methylphenidate were similar between users and non-users. Two potentially critical differences regarding the perceived availability between non-users and nonmedical users was that while the majority of the nonmedical users

thought methylphenidate is easy to obtain, non-users were most often unsure. Secondly, statistically more nonmedical users thought they could get methylphenidate from their friends than non-users who thought so. These two findings point to reasons why interest in use does not convert into actual methylphenidate use. A study conducted by Singh and colleagues (2014) reported that availability was a crucial factor preventing the conversion of interest into use. Additionally, numerous studies have also agreed that knowing a peer who uses prescription stimulants such as methylphenidate increases the risk of nonmedical use (Table 5-7).

Finally, as could be expected and in agreement with other publications (Habibzadeh *et al.,* 2011:73; Judson & Langdon, 2009:101), students who have used methylphenidate were significantly more knowledgeable about the drug than non-users. No significant difference was found between the medical and nonmedical users.

### 4.2 Limitations and strengths

This preliminary exploratory study was hindered by the small sample size as well as the study design. The population only included a relatively small sample of hostel students from one South African tertiary academic institution. Consequently, the generalisability of the results is limited to hostel students and the results are also not generalisable to hostel students from other South African academic institutions. Secondly, since it was a cross-sectional study, associations could be identified but no causalities could be determined. The study also carries the risk of nonresponse-bias since the response rate was relatively low (estimated at 14%). Finally, the study relied solely on self-reported data, therefore none of the data can be verified.

In spite of these limitations, the high degree of similarity between several of the results from this study and other similar studies conducted from around the world gives the results weight and credibility. The study had several important implications. The participating tertiary academic institution gained a better understanding of the pattern of methylphenidate use by the students who study at the institution. As a result of this study the safe use of methylphenidate was promoted. Students from this tertiary academic institution were given information relating to methylphenidate use, including the dangers thereof and legal implications. Furthermore, the insight provided by this study can aid healthcare workers in the encouragement of safer and more efficacious medicine use by the public. It also highlighted the need to improve the control of methylphenidate in South Africa.

### 4.3 Recommendations

Even though this study uncovered many meaningful results, much research is still needed to conceptualise the topic of nonmedical prescription drug use and diversion, especially in South Africa. Specifically, more research is required to verify if the results of this study are

generalisable to all South African universities. It is also worth exploring the extent of nonmedical methylphenidate use among university students in general. Furthermore, there is a gap in published literature when it comes to diversion of pharmaceuticals in South Africa. Future studies could consider the involvement of healthcare professionals in drug diversion. A final recommendation is that the off-label prescription practices of methylphenidate should be investigated and critically evaluated in light of the best clinical evidence.

## 4.4 Chapter summary

Chapter 4 summarised brief conclusions based on the literature and empirical objectives. In addition the limitations and strengths of the study were discussed. Finally recommendations were made for future research. Hereby the final chapter of this dissertation is concluded.

# ANNEXURE A: SUMMARY OF STUDIES FOR THE LITERATURE REVIEW

**Table 5-1: The prevalence of nonmedical use of methylphenidate and similar drugs by university students**

| Study | Inception year | Method | Location | Population | Sample size | Response rate (%) | Drug measured | Lifetime prevalence (%) | Past year prevalence (%) | Past month prevalence (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Babcock & Byrne (2000) | NR | Questionnaire (mailed) | USA (Massachusetts College of Liberal Arts) | College students (median age 21 years) | 283 | 20 | MPH | 16 | | |
| Benham *et al.* (2006) | NR | Questionnaire | USA (University of Texas-Pan American) | Students (mean age 21.9 years) | 146 | 97.3 | Ritalin® and other prescription stimulants | | 1.4 (Ritalin®), 6.8 (all) | |
| Benotsch *et al.* (2011) | NR | Questionnaire | USA (a mid-sized university in the Rocky Mountain region) | University students (mean age 20.5 years) | 435 | >90 | Ritalin®, Concerta® and other prescription stimulants | 5.3 (Ritalin®), 1.4 (Concerta®), 14.7 (all) | | |
| Clegg-Kraynok *et al.* (2011) | 2007 | Web-based survey | USA | College students (mean age 20.0 years) | 492 | NR | MPH and prescription stimulants | 22.5 (MPH), 14.4 (all) | 7 (MPH) | 8.5 (MPH) |

**Table 5-1: The prevalence of nonmedical use of methylphenidate and similar drugs by university students**

| Study | Inception year | Method | Location | Population | Sample size | Response rate (%) | Drug measured | Lifetime prevalence (%) | Past year prevalence (%) | Past month prevalence (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| DuPont *et al.* (2008) | NR | Web-based survey | USA | College students (aged 18-24 years) | 2 087 | NR | MPH | 5.3 | 24.5% (of lifetime users) | 13.6% (of lifetime users) |
| Eslami *et al.* (2014) | NR | Questionnaire | Iran (Isfahan University of Medical Sciences) | Medical students (mean age 23.02 years) | 241 | 91.2 | Ritalin® | 6.6 | 5.8 | 3.7 |
| Finger *et al.*[17] (2013) | 1990-2011 | Systematic research on four databases | N/A | College students | N/A | N/A | MPH | 8.3-9 | 3-16 | |
| Habibzadeh *et al.* (2011) | 2007 | Questionnaire | Iran (Tabriz University of Medical Sciences) | Medical students (mean age 21.4 years) | 310 | 62 | MPH | 8.7 | 74% (of lifetime users) | 11% (of lifetime users) |
| Johnston *et al.* (2013) | 2012 | Questionnaire | USA | College students | 580 | NR | Ritalin® | | 1.8 | |

[17] This review was included since it reviewed studies that were not accessible to the researcher because they were written in foreign languages. However, the review also included two studies included in this table: the study by Habibzadeh et al., 2011 and Teter et al., 2006.

**Table 5-1: The prevalence of nonmedical use of methylphenidate and similar drugs by university students**

| Study | Inception year | Method | Location | Population | Sample size | Response rate (%) | Drug measured | Lifetime prevalence (%) | Past year prevalence (%) | Past month prevalence (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Kerber & Wallisch (1999) | 1997 | Telephonic interviews | USA (7 large public universities and 3 large private universities in Texas) | Undergraduates (aged 18-26 years) | 2 420 | 89 | Ritalin® | 2 | 1.5 | |
| Low & Gendaszek (2002) | NR | Questionnaire | USA (small college) | Psychology undergraduate students (mean age 20.1 years) | 150 | 93.8 | MPH and prescription stimulants | | 7.3 (MPH), 35 (all) | 10 (all) |
| Mache *et al.* (2012) | 2010-2011 | Web-based survey | Germany | Students (mean age 24.58 years) | 1 053 | 61 | MPH and other cognitive enhancers | 2.2 (MPH), 0.1-22 (all) | | |
| Maier *et al.* (2013) | 2013 | Web-based survey | Switzerland (3 universities) | University students (mean age 23.18 years) | 6 275 | 22.3 | MPH | 5.8 | | 2.6[18] |

[18] This is the past month prevalence for cognitive enhancement only, not all reasons for nonmedical use.

**Table 5-1: The prevalence of nonmedical use of methylphenidate and similar drugs by university students**

| Study | Inception year | Method | Location | Population | Sample size | Response rate (%) | Drug measured | Lifetime prevalence (%) | Past year prevalence (%) | Past month prevalence (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Mazanov *et al.* (2013) | 2011 | Web-based survey | Australia (four south-eastern universities) | University students (mean age 23.9 years) | 1 729 | NR | MPH and other prescription stimulants | 7.7 (MPH), 8.5 (all) | | |
| Micoulaud-Franchi *et al.* (2014) | 2012-2013 | Web-based survey | France | Medicine and pharmacy students (mean age 21.04 years) | 206 | NR | MPH and other cognitive enhancers | | 3.6 (MPH), 67.4 (CE) | |
| Moore *et al.* (2014) | NR | Three web-based surveys | USA (a private, liberal arts college in the Pacific Northwest) | Undergraduate students (mean age 20.14 years) | 627, 468 & 400 | NR | MPH and other prescription stimulants | 8.5 (MPH), 11.7 (AMP), 18 (all) | | |
| Peralta & Steele (2010) | 2006 | Questionnaire | USA (Midwestern College of Arts and Sciences) | Undergraduates | 465 | NR | Ritalin® and other prescription stimulants | 11.6 (Ritalin®), 26 (all) | | |
| Silveira *et al.* (2014) | NR | Questionnaire | Brazil | Medical students (mean age 25.18 years) | 152 | 100 | MPH | 23.02 | | |

**Table 5-1: The prevalence of nonmedical use of methylphenidate and similar drugs by university students**

| Study | Inception year | Method | Location | Population | Sample size | Response rate (%) | Drug measured | Lifetime prevalence (%) | Past year prevalence (%) | Past month prevalence (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Singh *et al.* (2014) | 2012 | Web-based survey | UK and Ireland (104 universities) | University students (mean age 22.7 years) | 877 | NR | MPH | 5.9 | | |
| Srnick (2007) | NR | Questionnaire | USA (large mid-western university) | Undergraduates (mean age 20.42 years) | 465 | NR | Ritalin® and other prescription stimulants | 11.2 (Ritalin®) 26 (all) | | |
| Teter *et al.* (2003) | 2001 | Web-based survey | USA (University of Michigan) | Undergraduate students (mean age 20.07 years) | 2 250 | 64 | MPH | | 3 | |
| Castaldi *et al.* (2012) | 2010 | Questionnaire | Italy | University students (mean age 22.8 years) | 77 | NR | Cognitive enhancers | 16 | | |
| Dietz *et al.* (2013) | NR | Questionnaire (using the randomised response technique) | Germany (Johannes Gutenberg University) | Students (mean age 22.0 years) | 2 569 | 90.7 | Cognitive enhancers | | 20* | |
| Hupli (2013) | 2013 | Web-based survey | Netherlands (Amsterdam) | University students | 113 | NR | Cognitive enhancers | 12* | | |

* This study only measured the prevalence of use for cognitive enhancement, not all nonmedical use.

**Table 5-1: The prevalence of nonmedical use of methylphenidate and similar drugs by university students**

| Study | Inception year | Method | Location | Population | Sample size | Response rate (%) | Drug measured | Lifetime prevalence (%) | Past year prevalence (%) | Past month prevalence (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Ott & Biller-Andorno (2014) | 2011 | Web-based survey | Switzerland (University of Zürich) | Undergraduate and graduate students | 1 765 | 11-15 | Cognitive enhancers | 6.2* | | |
| Sattler & Wiegel (2013) | 2010 | Web-based survey | Germany (4 universities) | University students (median age 22-23 years) | 5 882 | 53.5 | Cognitive enhancers | 4.56* | 3.22* | 1.15* |
| Sattler *et al.* (2014) | 2011 | Web-based survey | Germany (4 universities) | University students (median age 22-23 years) | 3 486 | 69.1 | Cognitive enhancers | 2.8* | | |
| Wolff *et al.* (2014) | NR | Web-based survey | Germany (71 universities) | University students (mean age 23.56 years) | 1 007 | NR | Cognitive enhancers | 5.8* | | |
| Advokat *et al.* (2008) | 2004-2005 | Questionnaire | USA (Louisiana State Universities) | Undergraduates (mean age 21 years) | 1 550 | NR | ADHD medications | 43 | | |

* This study only measured the prevalence of use for cognitive enhancement, not all nonmedical use.

**Table 5-1: The prevalence of nonmedical use of methylphenidate and similar drugs by university students**

| Study | Inception year | Method | Location | Population | Sample size | Response rate (%) | Drug measured | Lifetime prevalence (%) | Past year prevalence (%) | Past month prevalence (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Carroll *et al.* (2006) | NR | Questionnaire | USA (New England private liberal arts college) | College students (mean age 19.2 years) | 347 | ±80 | ADHD medications | 9.2 | | |
| DeSantis *et al.* (2008) | 2005-2006 | Questionnaire | USA (large south-eastern university) | Undergraduates | 1 811 | NR | ADHD medications | 34 | | |
| Hall *et al.* (2005) | NR | Questionnaire | USA (mid-western university) | College students (mean age 19.38 years) | 381 | NR | ADHD medications | 13.7 | | |
| Novak *et al.* (2007) | 2005 | Web-based survey | USA (national, including 50 states) | Students (aged 18-25 years) | 4 297 | 3.8 | ADHD medications | 7.07 | 4.6 | |
| Peterkin *et al.* (2011) | 2009 | Questionnaire | USA (a large public university in northern Virginia) | College students (aged 18-30 years) | 184 | NR | ADHD medications | 25 | | |
| Van Eck *et al.* (2012) | NR | Web-based survey | USA | Psychology students (mean age 20.23 years) | 660 | NR | ADHD medication | 23 | | |

**Table 5-1: The prevalence of nonmedical use of methylphenidate and similar drugs by university students**

| Study | Inception year | Method | Location | Population | Sample size | Response rate (%) | Drug measured | Lifetime prevalence (%) | Past year prevalence (%) | Past month prevalence (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Arria, Caldeira, O'Grady, Vincent, Johnson, *et al.* (2008) | 2004-2009 | Cohort study (The College Life Study) | USA (large public mid-Atlantic university) | Undergraduates (aged 17-20 years in their 1st year at college) | 1 253 | N/A | Prescription stimulants | 13.5 | 10.4 | |
| Arria, Caldeira, O'Grady, Vincent, Fitzelle, *et al.* (2008) | 2004-2010 | Cohort study (The College Life Study) | USA (large public mid-Atlantic university) | Undergraduates (in their 2nd year at college) | 1 253 | N/A | Prescription stimulants | 22.6 | | |
| Bavarian (2012) & Bavarian *et al.* (2013) | 2011 | Questionnaire | USA (Oregon State University) | Undergraduates (mean age 21.44 years) | 520 | 96.3 | Prescription stimulants | 28.27 | | |
| Bavarian, Flay, Ketcham, *et al.* (2014) & Bavarian, Flay & Smit, (2014) | 2009 | Mixed (paper and web-based questionnaire) | USA (18 geographically diverse universities) | Undergraduates (under the age of 25) | 10 220 | 82 | Prescription stimulants | | 10.70 (range 0.33-20.04) | |

**Table 5-1: The prevalence of nonmedical use of methylphenidate and similar drugs by university students**

| Study | Inception year | Method | Location | Population | Sample size | Response rate (%) | Drug measured | Lifetime prevalence (%) | Past year prevalence (%) | Past month prevalence (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Bennett *et al.* (2014) | NR | Web-based survey | UK (North Wales) | University students (mean age 31.7 years) | 558 | 11 | Prescription stimulants | 6 | | |
| Checton & Greene (2011) | NR | Questionnaire | USA (large north-eastern university) | College students (mean age 20.04 years) | 720 | NR | Prescription stimulants | 31 | | |
| Dussault & Weyandt (2013) | 2010 | Web-based survey | USA (5 universities from north-eastern, south-eastern, north-western, south-western, and mid-western regions) | Undergraduate students | 1 033 | NR | Prescription stimulants | 19.8 | | |
| Egan *et al.* (2013) | 2009 | Web-based survey (The Study to Prevent Alcohol Related Consequences) | USA (8 universities in North Carolina) | Undergraduates (mean age 20 years) | 4 020 | 34.8 | Prescription stimulants | 10.6 | | |

**Table 5-1: The prevalence of nonmedical use of methylphenidate and similar drugs by university students**

| Study | Inception year | Method | Location | Population | Sample size | Response rate (%) | Drug measured | Lifetime prevalence (%) | Past year prevalence (%) | Past month prevalence (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Emanuel *et al.* (2013) | 2011 | Web-based survey | USA (4 Chicago-area medical schools) | Medical students (mean age 25.1 years) | 1 115 | 41 | Prescription stimulants | 18 | | |
| Ford & Schroeder (2009) | 1999 | Questionnaire (mailed) (Harvard School of Public Health's College Alcohol Study) | USA (119 colleges in 39 states) | Undergraduates (mean age 21 years) | 11 215 | NR | Prescription stimulants | | 4 | 2 |
| Franke *et al.* (2011) | 2009-2010 | Questionnaire | Germany (University of Mainz) | University students (mean age 24 years) | 512 | 68.3 | Prescription stimulants | 0.78* | 0.20* | 0* |
| Gallucci *et al.* (2014) | NR | Questionnaire | USA (large south-eastern university) | Undergraduates (mean age 19.6 years) | 1 020 | NR | Prescription stimulants | 35 | | 12 |
| Garnier-Dykstra *et al.* (2012) | 2004-2009 | Cohort study (The College Life Study) | USA (large public mid-Atlantic region university) | Undergraduates (in their 3rd and 4th year at college) | 1 253 | N/A | Prescription stimulants | 31.0 (4th year) | 16.1 (4th year), 20.1 (3rd year) | |

* This study only measured the prevalence of use for cognitive enhancement, not all nonmedical use.

**Table 5-1: The prevalence of nonmedical use of methylphenidate and similar drugs by university students**

| Study | Inception year | Method | Location | Population | Sample size | Response rate (%) | Drug measured | Lifetime prevalence (%) | Past year prevalence (%) | Past month prevalence (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Herman *et al.* (2011) | NR | Paper-based and web-based questionnaires | USA (northeast) | Medical and health profession students | 308 | 34.3 | Prescription stimulants | 10.4 | | |
| Holloway & Bennett (2012) | 2009 | Web-based survey | UK (South Wales) | University students | 1 614 | 19 | Prescription stimulant | 3 or less | | |
| Jeffers & Benotsch (2014) | 2012 | Web-based survey | USA (large eastern university) | Undergraduates (mean age 18.84 years) | 707 | NR | Prescription stimulants | 14.9 | | |
| Jeffers *et al.* (2013) | 2011 | Web-based survey | USA (large eastern university) | Undergraduates of psychology (mean age 19.92 years) | 705 | NR | Prescription stimulants | 11.7[19] | | |
| Judson & Langdon (2009) | NR | Web-based survey | USA (two small New England colleges) | College students (mean age 19.78 years) | 333 | 10 | Prescription stimulants | 20 | | |

[19] This study only measured the prevalence of use for weight loss, not all nonmedical use.

**Table 5-1: The prevalence of nonmedical use of methylphenidate and similar drugs by university students**

| Study | Inception year | Method | Location | Population | Sample size | Response rate (%) | Drug measured | Lifetime prevalence (%) | Past year prevalence (%) | Past month prevalence (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Kenna & Wood (2004) | 2000 | Questionnaire | USA (mid-sized north-eastern public university) | Pharmacy students (mean age 22.2 years) | 191 | 45.5 | Stimulants | 8 | | 3.5 |
| | | | | Nursing students (mean age 24.8 years) | 191 | 26.7 | | 11.8 | | 5.9 |
| Kilmer *et al.* (2015) | NR | Web-based survey | USA (a large public university in the Pacific Northwest) | Undergraduates (mean age 20.4 years) | 1 106 | NR | Prescription stimulants | 19 | | |
| Looby *et al.* (2014) | NR | Questionnaire | USA (a large north-eastern university) | Psychology students (mean age 19.03 years) | 91 | NR | Prescription stimulants | 37.4 | | |
| Lookatch *et al.* (2012) | 2009 | Questionnaire | USA (mid-Atlantic university) | Undergraduates (mean age 19.4 years) | 206 | NR | Prescription stimulants | | 26.1 | |
| Lord *et al.* (2009) | 2006 | Web-based survey | USA (private urban college) | Pharmacy students (mean age 20 years) | 1 538 | 62 | Prescription stimulants | 6.7 | 5.0 | |

**Table 5-1: The prevalence of nonmedical use of methylphenidate and similar drugs by university students**

| Study | Inception year | Method | Location | Population | Sample size | Response rate (%) | Drug measured | Lifetime prevalence (%) | Past year prevalence (%) | Past month prevalence (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| McCabe & Teter (2007); McCabe (2008a); McCabe (2008b) & McCabe *et al.* (2009) | 2005 | Web-based survey (College Student Life Survey) | USA (large mid-western university) | Undergraduates (mean age 19.9 years) | 3 639 | 68 | Prescription stimulants | 8.5 | 6 | |
| McCabe *et al.* (2005) & Ford (2008) | 2001 | Questionnaire (mailed) (Harvard School of Public Health's College Alcohol Study) | USA (119 US colleges in 39 US states) | Undergraduates | 10 904 | 52 (22-86) | Prescription stimulants | 6.9 | 4.1 | 2.1 |
| McCabe *et al.* (2014); McCabe *et al.* (2006a); McCabe *et al.* (2006b) & Teter *et al.* (2005) | 2003-2013 | Web-based survey (College Student Life Survey) | USA (large mid-western university) | Undergraduates (mean age overall 20 years) | 21771 (total) | 50 | Prescription stimulants | | | |
| | 2003 | | | | 9 906 | | | 8.1 | 5.4 | |
| | 2005 | | | | 3 629 | | | 8.5 | 6.0 | |
| | 2007 | | | | 1 740 | | | 9.6 | 6.8 | |
| | 2009 | | | | 1 088 | | | 9.6 | 6.9 | |
| | 2011 | | | | 1 469 | | | 10.7 | 7.6 | |
| | 2013 | | | | 3 939 | | | 12.7 | 9.3 | |

**Table 5-1: The prevalence of nonmedical use of methylphenidate and similar drugs by university students**

| Study | Inception year | Method | Location | Population | Sample size | Response rate (%) | Drug measured | Lifetime prevalence (%) | Past year prevalence (%) | Past month prevalence (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| McNiel *et al.* (2011) | 2008 | Questionnaire (mailed) | USA (south-central region) | Dental (fourth year) and dental hygiene students (seniors) (mode 24-26 years) | 243 | 61 | Prescription stimulants | 12.4 | | |
| Meisel & Goodie (2015) | 2012-2013 | Web-based survey | USA (large South-eastern university) | Psychology students (mean age 19.2 years) | 279 | NR | Prescription stimulants | | 17.2 | |
| Messina *et al.* (2014) | NR | Web-based survey | USA (large south-eastern public university) | Undergraduates (mean age 20.51 years) | 1 016 | NR | Prescription stimulants | | 25.4 | |
| Rozenbroek & Rothstein (2011) | NR | Questionnaire | USA (urban mid-Atlantic university) | College students | 413 | 94 | Prescription stimulants | 7.8 | | |
| Sharp & Rosén (2007) | NR | Questionnaire | USA (large western public university) | Psychology undergraduate students (mean age 19.28 years) | 448 | NR | Prescription stimulants | 18 | | |

**Table 5-1: The prevalence of nonmedical use of methylphenidate and similar drugs by university students**

| Study | Inception year | Method | Location | Population | Sample size | Response rate (%) | Drug measured | Lifetime prevalence (%) | Past year prevalence (%) | Past month prevalence (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Shillington *et al.* (2006) | 2005 | Web-based survey | USA (large south-western public university) | Undergraduates (mean age 20.2 years) | 1 998 | 32 | Prescription stimulants | | 11.2 | 4.15 |
| Stock *et al.* (2013) | NR | Web-based survey (Study 1) | USA (Eastern) | Psychology students (mean age 19.43 years) | 555 | NR | Prescription stimulants | 25 | | |
| | NR | Web-based survey (Study 2) | USA (Eastern) | Psychology students (aged 18-25 years) | 166 | NR | Prescription stimulants | 33 | | |
| Stone & Merlo (2011) | 2008-2009 | Questionnaire | USA (University of Florida) | University students (mean age 20.01 years) | 383 | NR | Prescription stimulants | 12.4 | | |
| Teter *et al.* (2006) & Kaloyanides *et al.* (2007) | 2005 | Web-based survey | USA | College students (mean age 20 years) | 4 580 | 66 | Prescription stimulants | 8.3 | 5.9 | |
| Tuttle *et al.* (2010) | NR | Questionnaire | Unknown | Medical students | 388 | 84 | Prescription stimulants | 10.1 | | |

**Table 5-1: The prevalence of nonmedical use of methylphenidate and similar drugs by university students**

| Study | Inception year | Method | Location | Population | Sample size | Response rate (%) | Drug measured | Lifetime prevalence (%) | Past year prevalence (%) | Past month prevalence (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Underhill & Langdon (2013) | 2009 | Web-based survey | USA (a small north-eastern liberal arts college) | Undergraduates (mean age 20.82 years) | 96 | 11 | Prescription stimulants | 37 | | |
| Van Hal *et al.* (2013) | 2009 | Unknown | Belgium (Ghent and Antwerp) | University students | 18 000 | NR | Prescription stimulants | 6.9 | 4.3 | |
| Vidourek *et al.* (2010) | 2009 | Questionnaire | NR | University students | 363 | 100 | Prescription stimulants | 17.5 | | |
| Weyandt *et al.* (2009) | NR | Questionnaire | USA (large public north-eastern university) | College students | 390 | NR | Prescription stimulants | 27.2 | | 7.5 |
| White *et al.* (2006) | 2002 | Web-based survey | USA (University of New Hampshire) | Undergraduate students (majority traditionally aged) | 1 025 | 20 | Prescription stimulants | 16.2 | | |

**Table 5-1: The prevalence of nonmedical use of methylphenidate and similar drugs by university students**

| Study | Inception year | Method | Location | Population | Sample size | Response rate (%) | Drug measured | Lifetime prevalence (%) | Past year prevalence (%) | Past month prevalence (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Zullig & Divin (2012) | 2008 | Paper based and web-based questionnaires (American College Health Association National College Health Assessment)[20] | USA (40 universities, private and public, located in the north-eastern, mid-western, southern and western regions) | College students (aged 18-25 years) | 22 783 | 27[21] | Prescription stimulants | | 5.9 | |

[20] American College Health Association, 2009.
[21] The response rate for the paper survey was 63% and that of the web-based survey was 22%.

ADHD = Attention-deficit/hyperactivity disorder
AMP = Amphetamine and dexamphetamine
CE = Cognitive enhancers
MPH = Methylphenidate
NR = Not reported
N/A = Not applicable
UK = United Kingdom
US = United States
USA = United States of America

**Table 5-2: Summary of products studied under the group name "methylphenidate"**

| Study | Methylphenidate | | | | |
|---|---|---|---|---|---|
| | **Concerta®** | **Focalin®[22]** | **Metadate®** | **Methylin®** | **Ritalin®** |
| Babcock & Byrne (2000) | | | | | X |
| DuPont *et al.* (2008) | X | X | X | X | X |
| Eslami *et al.* (2014) | | | | | X |
| Finger *et al.* (2013) | PNR | | | | |
| Habibzadeh *et al.* (2011) | PNR | | | | |
| Johnston *et al.* (2013) | | | | | X |
| Kerber & Wallisch (1999) | | | | | X |
| Maier *et al.* (2013) | PNR | | | | |
| Silveira *et al.* (2014) | PNR | | | | |
| Singh *et al.* (2014) | PNR | | | | |
| Teter *et al.* (2003) | | | | | X |

[22] The active ingredient of Focalin is dexmethylphenidate.

PNR = Product not reported

**Table 5-3: Summary of products studied under the group name "cognitive enhancers"**

| Study | Methylphenidate | | | | | | | Amphetamines | | | Modafinil | | Caffeine pills | β-blockers | Other |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Concerta® | Daytrana® | Equasym® | Focalin®[23] | Medikinet® | Metadate® | Ritalin® | Adderall® | Desoxyn® | Dexedrine® | Modasomil® | Provigil® | | | |
| Castaldi *et al.* (2012) | PNR | | | | | | | | | | | | | | |
| Dietz *et al.* (2013) | PNR | | | | | | | PNR | | | PNR | | X | X | Mephedrone |
| Hupli (2013) | X | | | | | | X | X | | | PNR | | | | Oxazepam, lorazepam and diazepam |
| Mache *et al.* (2012) | X | | | | | | X | X | X | X | | X | X | X | Fluoxetine, piracetam, phytomedicine, cocaine and cannabis/ marijuana |
| Micoulaud-Franchi *et al.* (2014) | PNR | | | | | | | PNR | | | PNR | | X | | Piracetam and Vitamin C |
| Ott & Biller-Andorno (2014) | X | X | X | X | X | X | X | X | | | X | X | | | |
| Sattler & Wiegel (2013) | PNR | | | | | | | PNR | | | PNR | | | | Piracetam and donepezil |
| Sattler *et al.* (2014) | PNR | | | | | | | | | | | | | | |
| Schelle *et al.* (2015) | | | | | | | X | | | | | X | | X | Rivastigmine (Exelon®) |
| Wolff *et al.* (2014) | PNR | | | | | | | | | | | | | | |

[23] The active ingredient of Focalin® is dexmethylphenidate.

PNR = Product not reported

**Table 5-4: Summary of products studied under the group name "ADHD medications"**

| Study | Methylphenidate | | | | | Amphetamines | | | | | | Modafinil | Pemoline | Atomoxetine |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Concerta® | Focalin®[24] | Metadate® | Methylin® | Ritalin® | Adderall® | Biphetamine® | Desoxyn® | Dexampex® | Dexedrine® | Dextrostat® | | Cylert® | Strattera® |
| Advokat *et al.* (2008) | X | | | | X | X | | | | X | | | | X |
| Carroll *et al.* (2006) | X | | | | X | X | | | | | | | | |
| DeSantis *et al.* (2008) | PNR | | | | | | | | | | | | | |
| Hall *et al.* (2005) | X | | X | | X | X | | X | | X | | | | |
| Novak *et al.* (2007) | X | X | | X | X | X | X | | X | X | X | X | X | X |
| Peterkin *et al.* (2011) | X | | | | X | X | | | | | | | | |
| Van Eck *et al.* (2012) | | | | | X | X | | | | X | | | X | |

[24] The active ingredient of Focalin is dexmethylphenidate.

PNR = Product not reported

**Table 5-5: Summary of products studied under the group name "prescription stimulants"**

| Study | Methylphenidate | | | | | | Amphetamines | | | | | | | | Modafinil | | | | | Pemoline | Phentermine | | Ephedrine |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Concerta® | Daytrana® | Focalin®[25] | Metadate® | Methylin® | Ritalin® | Adderall® | Benzedrine® | Biphetamine® | Desoxyn® | Dexamyl® | Dexedrine® | Dextrostat® | Vyvanse® | Alertec® | Modalert® | Modavigil® | Nuvigil®[26] | Provigil® | Cyclert® | Duramine® | Ionamin® | |
| Arria, Caldeira, O'Grady, Vincent, Fitzelle, *et al.* (2008) | PNR | | | | | | | | | | | | | | | | | | | | | | |
| Arria, Caldeira, O'Grady, Vincent, Johnson, *et al.* (2008) | PNR | | | | | | PNR | | | | | | | | | | | | | | | | |
| Bavarian (2012) & Bavarian *et al.* (2013) | X | X | X | X | X | X | X | | | | | X | X | X | | | | | | | | | |
| Bavarian, Flay, Ketcham, *et al.* (2014) & Bavarian, Flay & Smit, (2014) | | | | | | X | X | | | | | | | | | | | | | | | | |
| Benham *et al.* (2006) | | | | | | X | X | | | | | X | | | | | | | | | | | |
| Bennett *et al.* (2014) | | | | | | X | | | | | | | | | | | | | | | | | |
| Benotosh *et al.* (2011) | X | | | | | X | X | | | | | X | | | | | | | | | | | |
| Checton & Greene (2011) | | | | | | X | X | | | | | | | | | | | | | | | | |
| Clegg-Kraynok *et al.* (2011) | | | | | | X | X | | | | | X | X | | | | | X | X | | | | |
| Dussault & Weyandt (2013) | X | | | X | | X | X | | | | | X | | | | | | | | | | | |
| Egan *et al.* (2013) | X | | | | | X | X | | | | | X | | | | | | | | | | | |
| Emanuel *et al.* (2013) | X | | X | | | X | X | | | | | X | | X | | | | | | | | | |

[25] The active ingredient of Focalin is dexmethylphenidate.
[26] The active ingredient of Nuvigil® is armodafinil

**Table 5-5: Summary of products studied under the group name "prescription stimulants"**

| Study | Methylphenidate | | | | | | Amphetamines | | | | | | | | Modafinil | | | | | Pemoline | Phentermine | | Ephedrine |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Concerta® | Daytrana® | Focalin®[25] | Metadate® | Methylin® | Ritalin® | Adderall® | Benzedrine® | Biphetamine® | Desoxyn® | Dexamyl® | Dexedrine® | Dextrostat® | Vyvanse® | Alertec® | Modalert® | Modavigil® | Nuvigil®[26] | Provigil® | Cyclert® | Duramine® | Ionamin® | |
| Ford & Schroeder (2009) | PNR | | | | | | | | | | | | | | | | | | | | | | |
| Franke *et al.* (2011) | X | | | | | X | X | | | | | | | | PNR | | | | | | | | |
| Gallucci *et al.* (2014) | PNR | | | | | | | | | | | | | | | | | | | | | | |
| Garnier-Dykstra *et al.* (2012) | PNR | | | | | | | | | | | | | | | | | | | | | | |
| Herman *et al.* (2011) | X | | | | | X | X | | | | | | | | X | X | X | | X | | | | |
| Holloway & Bennett (2012) | | | | | | X | X | | | | | X | | | | | | | | | | | X |
| Jeffers & Benotsch (2014) | | | | | | X | X | | | | | | | | | | | | | | | | |
| Jeffers *et al.* (2013) | | | | | | X | X | | | | | | | | | | | | | | | | |
| Judson & Langdon (2009) | X | | | X | X | X | X | | | X | | X | | | | | | | | X | | | |
| Kenna & Wood (2004) | PNR | | | | | | | | | | | | | | | | | | | | | | |
| Kilmer *et al.* (2015) | X | | | | | X | X | | | | | X | | | | | | | | | | | |
| Looby *et al.* (2014) | X | | | | | X | X | | | | | | | | | | | | | | | | |
| Lookatch *et al.* (2012) | PNR | | | | | | | | | | | | | | | | | | | | | | |
| Lord *et al.* (2009)[27] | X | | | | | X | X | | | | | X | | | | | | | | | | | X |
| Low & Gendaszek (2002) | PNR | | | | | | PNR | | | | | | | | | | | | | | | | |

[27] This study also included atomoxetine as an option under "prescription stimulant"; however, atomoxetine is excluded from the table since it is considered a non-stimulant (Corman *et al.,* 2004:2398).

**Table 5-5: Summary of products studied under the group name "prescription stimulants"**

| Study | Methylphenidate | | | | | | Amphetamines | | | | | | | | Modafinil | | | | | Pemoline | Phentermine | | Ephedrine |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Concerta® | Daytrana® | Focalin®[25] | Metadate® | Methylin® | Ritalin® | Adderall® | Benzedrine® | Biphetamine® | Desoxyn® | Dexamyl® | Dexedrine® | Dextrostat® | Vyvanse® | Alertec® | Modalert® | Modavigil® | Nuvigil®[26] | Provigil® | Cyclert® | Duramine® | Ionamin® | |
| Mazanov *et al.* (2013) | | | | | | X | X | | | | | | | | | | | | | | X | | |
| McCabe & Teter (2007); McCabe (2008a); McCabe (2008b) & McCabe *et al.* (2009) | X | | | | | X | X | | | | | X | | | | | | | | | | | |
| McCabe *et al.* (2005) & Ford (2008) | | | | | | X | X | | | | | X | | | | | | | | | | | |
| McCabe *et al.* (2014); McCabe *et al.* (2006a); McCabe *et al.* (2006b) & Teter *et al.* (2005) | X | | | | | X | X | | | | | X | | | | | | | | | | | |
| McNiel *et al.* (2011) | X | | | | | X | X | | | | | | | | | | | | | | | | |
| Meisel & Goodie (2015) | | | | | | X | X | | | | | X | | | | | | | | | | | |
| Messina *et al.* (2014) | PNR | | | | | | | | | | | | | | | | | | | | | | |
| Moore *et al.* (2014) | X | | | X | X | X | X | | | | | | | | | | | | | | | | |
| Peralta & Steele (2010) | X | | | | | X | X | | | | | X | | | | | | | | | | X | |
| Rozenbroek & Rothstein (2011) | X | | | | | X | X | | | | | | | | | | | | | | | | |
| Sharp & Rosén (2007) | X | | | X | | X | X | | | | | X | | | | | | | | | | | |
| Shillington *et al.* (2006) | | | | | | X | X | | | | | | | | | | | | | | | | |
| Srnick (2007) | | | | | | X | X | | | | | | | | | | | | | | | | |

**Table 5-5: Summary of products studied under the group name "prescription stimulants"**

| Study | Methylphenidate | | | | | | Amphetamines | | | | | | | | Modafinil | | | | | Pemoline | Phentermine | | Ephedrine |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Concerta® | Daytrana® | Focalin®[25] | Metadate® | Methylin® | Ritalin® | Adderall® | Benzedrine® | Biphetamine® | Desoxyn® | Dexamyl® | Dexedrine® | Dextrostat® | Vyvanse® | Alertec® | Modalert® | Modavigil® | Nuvigil®[26] | Provigil® | Cyclert® | Duramine® | Ionamin® | |
| Stock *et al.* (2013) | X | | | | | X | X | | | | | | | | | | | | | | | | |
| Stone & Merlo (2011) | PNR | | | | | | | | | | | | | | | | | | | | | | |
| Sweeney *et al.* (2013)[28] | X | | X | X | X | X | X | | X | | X | X | X | | | | | | | | | | |
| Teter *et al.* (2006) & Kaloyanides *et al.* (2007) | X | | | X | X | X | X | X | | X | | | | | | | | | X | X | | | |
| Tuttle *et al.* (2010) | PNR | | | | | | PNR | | | | | | | | | | | | | | | | |
| Underhill & Langdon 2013 | X | | | | | X | X | | | | | X | | | | | | | | | | | |
| Van Hal *et al.* (2013) | PNR | | | | | | | | | | | | | | | | | | | | | | |
| Vidourek *et al.* (2010) | X | | | | | X | X | | | | | X | | | | | | | | | | | |
| Weyandt *et al.* (2009) | X | | | X | | X | X | | | | | X | | | | | | | | | | | |
| White *et al.* (2006) | X | | | | | X | X | | | | | X | | | | | | | | X | | | |
| Zullig & Divin (2012) | | | | | | X | X | | | | | | | | | | | | | | | | |

[28] This study described this group of drugs as "prescription stimulants for ADHD".

PNR = Product not reported

**Table 5-6: The difference between male and female nonmedical users of methylphenidate and similar drugs**

| Study | Drug group studied | Population (female proportion) | Statistical significance | Is there a significant difference between male and female users? |
|---|---|---|---|---|
| Arria, Caldeira, O'Grady, Vincent, Johnson, *et al.* (2008) | Prescription stimulants | Undergraduates (51.4%) | NR | No |
| Arria *et al.* (2013) | Prescription stimulants | Undergraduates (52.1%) | NR | No |
| Bavarian (2012) & Bavarian *et al.* (2013) | Prescription stimulants | Undergraduates (55.2%) | NR | No |
| Bavarian, Flay, Ketcham, *et al.* (2014) & Bavarian, Flay & Smit, (2014) | Prescription stimulants | Undergraduates (56.5%) | $p<0.01$ | No |
| Carroll *et al.* (2006) | ADHD medications | College students (59%) | NR | No |
| Castaldi *et al.* (2012) | Cognitive enhancers | University students (51/77) | $p<0.55$ | No |
| Clegg-Kraynok *et al.* (2011) | Prescription stimulants | College students | NR | No |
| DeSantis *et al.* (2008) | ADHD medications | Undergraduates (45%) | $p<0.001$ | Yes (M>F) |
| Dietz *et al.* (2013) | Cognitive enhancers | Students (58.7%) | NR | Yes (M>F) |
| DuPont *et al.* (2008) | MPH | College students | NR | No |
| Emanuel *et al.* (2013) | Prescription stimulants | Medical students (52%) | $p=0.007$ | Yes (M>F) |
| Eslami *et al.* (2014) | Ritalin® | Medical students | $p=0.001$ | Yes (M>F) |
| Franke *et al.* (2011) | Prescription stimulants | University students (611/1035) | $p=0.134$ | No |
| Gallucci *et al.* (2014) | Prescription stimulants | Undergraduates (68%) | NR | No |
| Garnier-Dykstra *et al.* (2012) | Prescription stimulants | Undergraduates (51%) | $p<0.05$ | Yes (M>F) |
| Habibzadeh *et al.* (2011) | MPH | Medical students (56.7%) | $p<0.001$ | Yes (M>F) |
| Hall *et al.* (2005) | ADHD medications | College students (53%) | $p<0.05$ | Yes (M>F) |
| Hartung *et al.* (2013) | Prescription stimulants | Undergraduates (65.2%) | $p=0.009$ | Yes (M>F) |

**Table 5-6: The difference between male and female nonmedical users of methylphenidate and similar drugs**

| Study | Drug group studied | Population (female proportion) | Statistical significance | Is there a significant difference between male and female users? |
|---|---|---|---|---|
| Herman *et al.* (2011) | Prescription stimulants | Medical and health profession students (53.1%) | NR | Yes (M>F) |
| Herman-Stahl *et al.* (2007) | Prescription stimulants | Adults | NR | No |
| Jeffers & Benotsch (2014) | Prescription stimulants | Undergraduates (69.8%) | $p$=0.07 | No |
| Jeffers *et al.* (2013) | Prescription stimulants | Undergraduates of psychology (61.3%) | $p$=0.166 | No |
| Johnston *et al.* (2013) | Ritalin® | College students | NR | Yes (M>F) |
| Kilmer *et al.* (2015) | Prescription stimulants | Undergraduates (656/1106) | NR | Yes (M>F) |
| Kroutil *et al.* (2006) | ADHD stimulants | Adults and adolescents aged 12 years and older | $p$<0.01 | Yes (M>F) |
| Lord *et al.* 2009 | Prescription stimulants | Pharmacy students (64%) | NR | No |
| Low & Gendaszek (2002) | Prescription stimulants | Psychology undergraduate students (74/150) | $p$<0.001 | Yes (M>F) |
| Mache *et al.* (2012) | Cognitive enhancers | Students (635/1053) | $p$>0.5 | No |
| Maier *et al.* (2013) | MPH | University students (gender distribution equal) | $p$=0.007 | Yes (M>F) |
| Mazanov *et al.* (2013) | Prescription stimulants | University students (53.2%) | $p$<0.01 | **Yes (M<F)** |
| McCabe & Teter (2007); McCabe (2008a); McCabe (2008b) & McCabe *et al.* (2009) | Prescription stimulants | Undergraduates (53.6%) | $p$<0.05 | Yes (M>F) |
| McCabe *et al.* (2005) & Ford (2008) | Prescription stimulants | Undergraduates | $p$<0.001 | Yes (M>F) |

**Table 5-6: The difference between male and female nonmedical users of methylphenidate and similar drugs**

| Study | Drug group studied | Population (female proportion) | Statistical significance | Is there a significant difference between male and female users? |
|---|---|---|---|---|
| McCabe *et al.* (2014); McCabe *et al.* (2006a); McCabe *et al.* (2006b) & Teter *et al.* (2005) | Prescription stimulants | Undergraduates (56%) | $p<0.01$ | Yes (M>F) |
| McNiel *et al.* (2011) | Prescription stimulants | Dental and dental hygiene students (69%) | NR | **Yes (M<F)** |
| Messina *et al.* (2014) | Prescription stimulants | Undergraduates (70.5%) | NR | No |
| Micoulaud-Franchi *et al.* (2014) | Cognitive enhancers | Medicine and pharmacy students (58.3%) | NR | No |
| Moore *et al.* (2014) | Prescription stimulants | Undergraduate students | NR | No |
| Novak *et al.* (2007) | ADHD medications | Adults (56.8%) | NR | No |
| Ott & Biller-Andorno (2014) | Cognitive enhancers | Undergraduate and graduate students (61.9%) | $p=0.029$ | Yes (M>F) |
| Peterkin *et al.* (2011) | ADHD medications | College students (88/184) | $p=0.0031$ | Yes (M>F) |
| Poulin (2007) | MPH | Adolescents (50%) | $p<0.001$ | Yes (M>F) |
| Rabiner *et al.* (2009b) | Prescription stimulants | College students with and without ADHD (61%) | $p<0.01$ | Yes (M>F) |
| Rozenbroek & Rothstein (2011) | Prescription stimulants | College students (45%) | NR | No |
| Sattler & Wiegel (2013) | Cognitive enhancers | University students | NR | No |
| Sharp & Rosén (2007) | Prescription stimulants | Psychology undergraduate students (63.2%) | NR | No |
| Shillington *et al.* (2006) | Prescription stimulants | Undergraduates (60%) | NR | No |
| Silveira *et al.* (2014) | MPH | Medical students (59.9%) | $p=0.366$ | No |
| Singh *et al.* (2014) | MPH | University students (53%) | $p<0.001$ | Yes (M>F) |

**Table 5-6: The difference between male and female nonmedical users of methylphenidate and similar drugs**

| Study | Drug group studied | Population (female proportion) | Statistical significance | Is there a significant difference between male and female users? |
|---|---|---|---|---|
| Sweeny *et al.* (2013) | ADHD stimulants | Adults and adolescents (aged 12 years or older) | NR | Yes (M>F) |
| Teter *et al.* (2003) | MPH | Undergraduate students | NR | No |
| Teter *et al.* (2006) & Kaloyanides *et al.* (2007) | Prescription stimulants | College students (50%) | NR | No |
| Tuttle *et al.* (2010) | Prescription stimulants | Medical students (44%) | NR | No |
| Underhill & Langdon (2013) | Prescription stimulants | Undergraduates (73%) | $p$=0.05 | Yes (M>F) |
| Van Eck *et al.* (2012) | ADHD medication | Psychology students (70%) | NR | No |
| Van Hal *et al.* (2013) | Prescription stimulants | University students | NR | Yes (M>F) |
| Volger *et al.* (2014) | Prescription stimulants | Pharmacy students | NR | No |
| Wasserman *et al.* (2014) | Prescription stimulants | Medical students (60.7%) | $p$<0.05 | Yes (M>F) |
| Weyandt *et al.* (2009) | Prescription stimulants | College students (71.6%) | NR | No |
| White *et al.* (2006) | Prescription stimulants | Undergraduate students (66%) | NR | No |

ADHD = Attention-deficit/hyperactivity disorder
F = Female
M = Male
MPH = Methylphenidate
NR = Not reported

**Table 5-7: Risk factors associated with the nonmedical use of methylphenidate and similar drugs**

| Study | Drug | Population | Gender | Race | Sorority/ Fraternity affiliation | Academic performance | Alcohol use | Illicit drug use | Other |
|---|---|---|---|---|---|---|---|---|---|
| Advokat *et al.* (2008) | ADHD medications | Undergraduates | | | | Low GPA | A | Marijuana | |
| Arria, Caldeira, O'Grady, Vincent, Johnson, *et al.* (2008) | Prescription stimulants | Undergraduates | NA | | | | A | Marijuana, inhalants, ecstasy, cocaine, hallucinogens, amphetamines, prescription analgesics & prescription tranquilisers | |
| Arria *et al.* (2013) | Prescription stimulants | Undergraduates | NA | | | Low GPA | A | Cannabis | Higher family income (mean US $78 600) & skipping class |
| Barrett *et al.* (2005) | MPH | University students | | | | | | Cannabis, ecstasy, cocaine, ephedrine, *d*-amphetamine & psilocybin ($p<0.01$) | |

**Table 5-7: Risk factors associated with the nonmedical use of methylphenidate and similar drugs**

| Study | Drug | Population | Gender | Race | Sorority/ Fraternity affiliation | Academic performance | Alcohol use | Illicit drug use | Other |
|---|---|---|---|---|---|---|---|---|---|
| Bavarian, Flay, Ketcham, *et al.* (2014) & Bavarian, Flay & Smit, (2014) | Prescription stimulants | Undergraduates | NA | White | A | Low GPA | A | Marijuana & cocaine | Nonreligious university attendance, past year depression, past year academic stress, financial stress & cigarette use |
| Bavarian (2012) & Bavarian *et al.* (2013) | Prescription stimulants | Undergraduates | NA | White | NA | Low GPA | | | ADHD diagnosis, perception of peer engagement in nonmedical use of prescription stimulants, financial stress & not participating in religious activities |
| Carroll *et al.* (2006) | ADHD medications | College students | NA | NA | | | | | Peer engagement in nonmedical use of prescription stimulants |
| Clegg-Kraynok *et al.* (2011) | Prescription stimulants | College students | NA | NA | A | Low GPA | | | Worse subjective quality of sleep & higher academic year |
| DeSantis *et al.* (2008) | ADHD medications | Undergraduates | Male | White | A | | | | Higher academic year |
| Dietz *et al.* (2013) | Cognitive enhancers | Students | Male | | | | | | Field of study is sport-related |

**Table 5-7: Risk factors associated with the nonmedical use of methylphenidate and similar drugs**

| Study | Drug | Population | Gender | Race | Sorority/ Fraternity affiliation | Academic performance | Alcohol use | Illicit drug use | Other |
|---|---|---|---|---|---|---|---|---|---|
| DuPont *et al.* (2008) | MPH | College students | NA | White | | | | | |
| Dussault & Weyandt (2013) | Prescription stimulants | Undergraduate students | | | A | | | | Peer engagement in nonmedical use of prescription stimulants, depression, anxiety, stress, internal impulsivity & internal restlessness |
| Emanuel *et al.* (2013) | Prescription stimulants | Medical students | Male | | | | | Marijuana, ecstasy & LSD | First years least likely |
| Eslami *et al.* (2014) | Ritalin® | Medical students | Male | | | | A | | Cigarette use & educational level (MD>BSc) |
| Franke *et al.* (2011) | Prescription stimulants | University students | NA | | A | | | Illicit stimulants | |
| Gallucci *et al.* (2014) [29] | Prescription stimulants | Undergraduates | NA | White | A | | | | Higher academic year |
| Garnier-Dykstra *et al.* (2012) | Prescription stimulants | Undergraduates | NA | NA | NA | Low GPA | | Cannabis | |

[29] The risk factors in this study apply to lifetime nonmedical use.

**Table 5-7: Risk factors associated with the nonmedical use of methylphenidate and similar drugs**

| Study | Drug | Population | Gender | Race | Sorority/ Fraternity affiliation | Academic performance | Alcohol use | Illicit drug use | Other |
|---|---|---|---|---|---|---|---|---|---|
| Habibzadeh *et al.* (2011) | MPH | Medical students | Male | | | Low mean grade | | | |
| Hall *et al.* (2005) | ADHD medications | College students | Male | | | | | | |
| Hartung *et al.* (2013) | Prescription stimulants | Undergraduates | Male | | | | | Marijuana, amphetamines, ecstasy, hallucinogens, pain medication & anxiety medication | Cigarette use, ADHD symptoms, high parental expectations & sensation seeking |
| Herman *et al.* (2011) | Prescription stimulants | Medical and health profession students | Male | White | | | | | |
| Herman-Stahl *et al.* (2007) | Prescription stimulants | Adults | NA | White | | | | Marijuana, cocaine/crack, inhalants, hallucinogens, heroin, narcotic analgesics, sedatives & tranquilizers | Current/past college enrolment, sensation seeking & psychological distress |

**Table 5-7: Risk factors associated with the nonmedical use of methylphenidate and similar drugs**

| Study | Drug | Population | Gender | Race | Sorority/ Fraternity affiliation | Academic performance | Alcohol use | Illicit drug use | Other |
|---|---|---|---|---|---|---|---|---|---|
| Jeffers & Benotsch (2014) | Prescription stimulants | Undergraduates | NA | NA | | NA[30] | A | Marijuana, cocaine, Meth, other amphetamines, sedatives, hallucinogens steroids, opioids, inhalants, MDMA, poppers, GHB, ketamine, rohypnol & mephedrone | Lower BMI, more disordered eating behaviours, lower body image & cigarette use |
| Jeffers *et al.* (2013) | Prescription stimulants | Undergraduates of psychology | NA | White | | | | | Lower self-esteem, poor coping with stressors, engagement in unhealthy weight loss behaviours & more disordered eating behaviours |
| Johnston *et al.* (2013) | Ritalin® | College students | Male | | | | | | |

[30] It should be borne in mind that this study only measured nonmedcial use of prescription stimulants for the purpose of weight loss.

**Table 5-7: Risk factors associated with the nonmedical use of methylphenidate and similar drugs**

| Study | Drug | Population | Gender | Race | Sorority/ Fraternity affiliation | Academic performance | Alcohol use | Illicit drug use | Other |
|---|---|---|---|---|---|---|---|---|---|
| Kilmer *et al.* (2015) | Prescription stimulants | Undergraduates | Male | | A | | A | | Normative perceptions of nonmedical use of prescription stimulants |
| Kroutil *et al.* (2006) | ADHD stimulants | Adults and adolescents aged 12 years and older | Male | White | | | | | Youth (aged 12-25 years) & low family income (less than US $10 000) |
| Lookatch *et al.* 2012 | Prescription stimulants | Undergraduates | | | | | A | | Positive outcome expectancy, sensation seeking, impulsivity & less negative evaluation |
| Lord *et al.* (2009) | Prescription stimulants | Pharmacy students | NA | White | A | Low academic achievers | A | Marijuana, cocaine, hallucinogens & tranquilisers | Older students (aged 21 years and older), off-campus housing, tobacco use & 3rd/ 4th/ 5th/ 6$^{th}$ academic year |
| Low & Gendaszek (2002) | Prescription stimulants | Psychology undergraduate students | Male | | | | | | Sensation seeking |
| Mache *et al.* (2012) | Cognitive enhancers | Students | NA | | | | | | |
| Maier *et al.* (2013) | MPH | University students | Male | | | | | | |

**Table 5-7: Risk factors associated with the nonmedical use of methylphenidate and similar drugs**

| Study | Drug | Population | Gender | Race | Sorority/ Fraternity affiliation | Academic performance | Alcohol use | Illicit drug use | Other |
|---|---|---|---|---|---|---|---|---|---|
| Maier *et al.* (2013) | Cognitive enhancers | University students | | | | | A | Cannabis, cocaine, amphetamine, GHB & ecstasy | Higher performance pressure |
| Mazanov *et al.* (2013) | Prescription stimulants | University students | Female | | | | | | Field of study (law or medicine) |
| McCabe & Teter (2007); McCabe (2008a) ; McCabe (2008b) & McCabe *et al.* (2009) | Prescription stimulants | Undergraduates | Male | White | A | | A | A | Higher family income |
| McCabe *et al.* (2005) & Ford (2008) | Prescription stimulants | Undergraduates | Male | White | A | Low GPA | A | Marijuana, ecstasy & cocaine | Cigarette use & being a non-athlete |
| McCabe *et al.* (2014); McCabe *et al.* (2006a); McCabe *et al.* (2006b) & Teter *et al.* (2005) | Prescription stimulants | Undergraduates | Male | White | A | Low GPA | A | Marijuana, cocaine, ecstasy & hallucinogens | History of medical use of prescription drugs, higher academic year, Jewish religion or no religion (compared to Catholics) & first medical use in secondary school or college |
| McNiel *et al.* (2011) | Prescription stimulants | Dental and dental hygiene students | Female | | | | | | |

**Table 5-7: Risk factors associated with the nonmedical use of methylphenidate and similar drugs**

| Study | Drug | Population | Gender | Race | Sorority/ Fraternity affiliation | Academic performance | Alcohol use | Illicit drug use | Other |
|---|---|---|---|---|---|---|---|---|---|
| Messina *et al.* (2014) | Prescription stimulants | Undergraduates | NA | | | | A | | Impulsivity |
| Micoulaud-Franchi *et al.* (2014) | Cognitive enhancers | Medicine and pharmacy students | NA | | | | | | |
| Moore *et al.* (2014) | Prescription stimulants | Undergraduate students | NA | NA | NA | Low GPA | A | Cocaine (NA with marijuana use) | Procrastination and poor time management, normative perception regarding nonmedical use of prescription stimulants & nicotine and tobacco use |
| Novak *et al.* (2007) | ADHD medications | Adults | NA | NA | | | A | Marijuana | Young adults (aged 18-25 years) & ADHD diagnosis |
| Ott & Biller-Andorno (2014) | Cognitive enhancers | Undergraduate and graduate students | Male | | NA | NA | NA | Ecstasy, cocaine & LSD | Nonreligious |
| Peterkin *et al.* (2011) | ADHD medications | College students | Male | | | | | | ADHD symptoms |
| Poulin (2007) | MPH | Adolescents | Male | | | | A | Cannabis | Positive ADHD screening test, cigarette use & depressive symptoms |
| Rabiner *et al.* (2009a) | ADHD medications | College students with ADHD | | NA | NA | NA | A | Marijuana (cocaine NA) | Impulsivity |

**Table 5-7: Risk factors associated with the nonmedical use of methylphenidate and similar drugs**

| Study | Drug | Population | Gender | Race | Sorority/ Fraternity affiliation | Academic performance | Alcohol use | Illicit drug use | Other |
|---|---|---|---|---|---|---|---|---|---|
| Rabiner *et al.* (2009b) | ADHD medications | College students with and without ADHD | Male | White | A | Low GPA | A | Marijuana, cocaine & inhalants | Cigarette use, concern over academic performance & inattentive symptoms |
| Rozenbroek & Rothstein (2011) | Prescription stimulants | College students | NA | White | | | | CNS depressants & opioids | |
| Sattler & Wiegel (2013) | Cognitive enhancers | University students | NA | | | | | | Cognitive test anxiety, low expectation of side effects, low competency, risk attitude & older students |
| Sharp & Rosén (2007) | Prescription stimulants | Psychology undergraduate students | NA | NA | | | | A | |
| Shillington *et al.* (2006) | Prescription stimulants | Undergraduates | NA | NA | A | Low GPA | A | Marijuana, cocaine & ecstasy | Cigarette use & not being in a committed relationship |
| Silveira *et al.* (2014) | MPH | Medical students | NA | | | | A | | Fifth years are more likely to use than sixth years |

**Table 5-7: Risk factors associated with the nonmedical use of methylphenidate and similar drugs**

| Study | Drug | Population | Gender | Race | Sorority/ Fraternity affiliation | Academic performance | Alcohol use | Illicit drug use | Other |
|---|---|---|---|---|---|---|---|---|---|
| Singh *et al.* (2014) | MPH | University students | Male | | | | A | Cannabis | Older students, perception of peer engagement, ADHD symptoms & belief that nonmedical use is ethical |
| Sweeney *et al.* (2013) | ADHD stimulants | Adults and adolescents (aged 12 years or older) | Male | White | | | | | Young adults (<26 years) & unmarried |
| Teter *et al.* (2003) | MPH | Undergraduate students | NA | NA | NA | NA | A | Marijuana & ecstasy | Weekly party behaviour, experiencing adverse consequences related to alcohol and drug use |
| Teter *et al.* (2006) & Kaloyanides *et al.* (2007) | Prescription stimulants | College students | NA | White & Hispanic | | | | | |
| Tuttle *et al.* (2010) | Prescription stimulants | Medical students | NA | White | | | | | ADHD diagnosis NA; $p$=0.07 |
| Underhill & Langdon (2013) | Prescription stimulants | Undergraduates | Male | NA | | | | | Perception of peer engagement in nonmedical prescription stimulant use |
| Van Eck *et al.* (2012) | ADHD medication | Psychology students | NA | | | | | | ADHD symptoms & conduct problems |

**Table 5-7: Risk factors associated with the nonmedical use of methylphenidate and similar drugs**

| Study | Drug | Population | Gender | Race | Sorority/ Fraternity affiliation | Academic performance | Alcohol use | Illicit drug use | Other |
|---|---|---|---|---|---|---|---|---|---|
| Van Hal *et al.* (2013) | Prescription stimulants | University students | Male | | | | | | |
| Volger *et al.* (2014) | Prescription stimulants | Pharmacy students | NA | | A[31] | NA | A | Marijuana, cocaine, LSD, ecstasy & prescription drugs | Participation in sport, participation in joint degree programmes, nonmedical use of prescription stimulants before attending Pharmacy School & lower academic year |
| Wasserman *et al.* (2014) | Prescription stimulants | Medical students | Male | | NA | | A | A | Less negative perceptions |
| Weyandt *et al.* (2009) | Prescription stimulants | College students | NA | | A | Low GPA | | | Psychological distress, sensation seeking & internal restlessness |
| White *et al.* (2006) | Prescription stimulants | Undergraduate students | NA | | | | | | Private school attendance |

[31] According to this study, belonging to a fraternity is a protective factor against nonmedical use of prescription stimulants.

A = Associated
ADHD = Attention-deficit/hyperactivity disorder
BMI = Body mass index
GHB = Gamma hydroxybutyrate
GPA = Grade point average
LSD = Lysergic acid diethylamide
MDMA = 3,4-methylenedioxymethamphetamine
MPH = Methylphenidate
NA = Not associated

**Table 5-8: Percentage of nonmedical users who obtain methylphenidate and similar drugs from various sources**

| Study | Drug | Friends | Family | Acquaintance/ stranger | Prescription for falsified symptoms | Own valid prescription | Internet | Other |
|---|---|---|---|---|---|---|---|---|
| Arria, Caldeira, O'Grady, Vincent, Fitzelle, *et al.* (2008) & Arria, Caldeira, O'Grady, Vincent, Johnson, *et al.* (2008) | Prescription stimulants (year 1 of the College Life Study) | 78.7% (with Rx), 15.6% (without Rx), 6.7% (Rx status unknown) | 3.1% | 1.8% | | 1.8% | 0% | Stole from a pharmacy: 0.4%<br>Unknown: 0.4% |
| Barrett *et al.* (2005) | MPH | 77.8% (with Rx) | | | | | | Black-market: 16.7%<br>"Getting own Rx"[32]: 11.1%<br>Theft: 4% |
| Clegg-Kraynok *et al.* (2011) | Prescription stimulants | 59.2% (free), 17.6% (sold) | 8.8% | 39.7% | 1.5% | | | |
| DeSantis *et al.* (2008) | Prescription stimulants | 87% | | 8% | | 4% | | Significant others: 4% |
| Garnier-Dykstra *et al.* (2012) | Prescription stimulants (year 2 of the College Life Study) | 78.3% (with Rx), 21.3% (without Rx) | | | | 2.2% | 0% | 12.6% |
| | Prescription stimulants (year 3 of the College Life Study) | 77.4% (with Rx), 17.6% (without Rx) | | | | 5.3% | 0% | 8.3% |

[32] It is unclear whether these students had a diagnosis for ADHD or if they deceived healthcare workers in order to get the prescription.

**Table 5-8: Percentage of nonmedical users who obtain methylphenidate and similar drugs from various sources**

| Study | Drug | Friends | Family | Acquaintance/ stranger | Prescription for falsified symptoms | Own valid prescription | Internet | Other |
|---|---|---|---|---|---|---|---|---|
| | Prescription stimulants (year 4 of the College Life Study) | 73.9% (with Rx), 16.7% (without Rx) | | | | 8.1% | 0% | 8.1% |
| Jeffers & Benotsch (2014) | Prescription stimulants | 56.7% | 13.3% | 10% | | | 3.3% | |
| Lord *et al.* (2009) | Prescription stimulants | 75% | 9% (Parents), 8% (other family) | 28% | | | <2% | Work site: 6% |
| McCabe *et al.* (2006b) | Prescription stimulants | 67.7% | 3.1% | | | | 0% | Unknown: 28.6%; Other (abroad, drug dealer, and self): <1% |
| McNiel *et al.* (2011) | Prescription stimulants | 87% | 7% | | | | | Physicians: 7% |
| Novak *et al.* (2007) | ADHD medications | 65.8% (given for free) 13.0% (bought from) 34.5% (stole from) | | | 19.8% | | 5.2% | 10.3% |
| Silveira *et al.* (2014) | MPH | 71.4% (given for free) | | | | 25.1% | | 2.9% |
| Tuttle *et al.* (2010) | Prescription stimulants | 70% | | | | | | |

ADHD = Attention-deficit/hyperactivity disorder
Rx = Prescription
MPH = Methylphenidate

**Table 5-9: The prevalence of simultaneous use of other substances with methylphenidate and similar drugs by nonmedical users**

| Study | Drug studied | Simultaneous use with: | | | |
|---|---|---|---|---|---|
| | | Alcohol | Cannabis/ Marijuana | Cocaine | Miscellaneous drugs |
| Barrett *et al.* (2005) | MPH | 50% | 42% | 10% | Psilocybin (6%); Sedatives (4%); MDMA (4%); GHB (4%); Amphetamine (2%); Ephedrine (2%); Dexedrine (2%); LSD (2%) |
| Barrett *et al.* (2006) | MPH | 35.7% | 28.2% | | |
| Brandt *et al.* (2014) | Prescription stimulants | | 47.1% | | Other drugs (41.8%);<br>Of the nonmedical users who used prescription stimulants with other drugs, 86.8% mixed them with marijuana, 81.6% with alcohol, 10.5% with cocaine, 7.9% with ecstasy, and 5.3% with LSD |
| Darredeau *et al.* (2007) | MPH | 63% (12/19) | 53% (10/19) | 21% (4/19) | MDMA (4/19=21%); Psilocybin (3/19=16%); Amphetamine (2/19=11%) |
| Egan *et al.* (2013) | Prescription stimulants | 46.4% | | | |
| Low & Gendaszek (2002) | Prescription stimulants | 19.3% | | | |
| McCabe *et al.* (2015) | Prescription stimulants | 48.4% | 51.1% | | |
| Messina *et al.* (2014) | Prescription stimulants | 10.8% (N=110) | | | |
| Novak *et al.* (2007) | ADHD medications | 52.8% | 26.2% | 19.8% | Other prescription drugs such as pain relievers, tranquilisers or sleeping pills (19.5%); Heroin (6.4%); Hallucinogens (3.6%); Inhalants (0.9%) |

**Table 5-9: The prevalence of simultaneous use of other substances with methylphenidate and similar drugs by nonmedical users**

| Study | Drug studied | Simultaneous use with: | | | |
|---|---|---|---|---|---|
| | | Alcohol | Cannabis/ Marijuana | Cocaine | Miscellaneous drugs |
| Rabiner *et al.* (2009a) | ADHD medications | 30% (N=34) | 17% (N=19) | 0% | |
| Silveira *et al.* (2014) | MPH | 14.2% (N=5) | 2.8% (N=1) | 0% | |

ADHD = Attention-deficit/hyperactivity disorder
GHB = Gamma hydroxybutyrate
LSD = Lysergic acid diethylamide
MDMA = 3,4-methylenedioxymethamphetamine
MPH = Methylphenidate

# ANNEXURE B: PROOF OF SUBMISSION OF MANUSCRIPT ONE



## A manuscript number has been assigned: HSAG-D-15-00098

**From:** "Health SA Gesondheid" <healthsa@uj.ac.za>
**To:** Johanita.Burger@nwu.ac.za
**Date:** Tuesday - September 15, 2015 11:40 AM
**Subject:** A manuscript number has been assigned: HSAG-D-15-00098
**Attachments:** Mime.822

Ms. Ref. No.: HSAG-D-15-00098
Title: Appropriate and non-medical use of methylphenidate by South African university residence students: prevalence, reasons for use and adverse effects
Health SA Gesondheid-Journal of Interdisciplinary Health Sciences

Dear Dr. Burger,

Your submission "Appropriate and non-medical use of methylphenidate by South African university residence students: prevalence, reasons for use and adverse effects" has been assigned manuscript number HSAG-D-15-00098.

To track the status of your paper, please do the following:

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Kind regards,

Archie Zulu
Editorial Office
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# ANNEXURE C: PROOF OF SUBMISSION OF MANUSCRIPT TWO



## [SAMJ] Submission Acknowledgement

**From:** "Professor Janet Seggie" <janet.seggie@hmpg.co.za>
**To:** Johanita.Burger@nwu.ac.za
**Date:** Tuesday - September 22, 2015 10:05 AM
**Subject:** [SAMJ] Submission Acknowledgement
**Attachments:** Mime.822

Dear Johanita R Burger,

Thank you for submitting the manuscript, "Students' perception of the perceived availability and diversion of methylphenidate in a South African tertiary academic institution" to the South African Medical Journal. With the online journal management system that we are using, you will be able to track its progress through the editorial process by logging in to the journal web site:

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If you have any questions, please contact me. Thank you for considering this journal as a venue for your work.

Kind regards

Professor Janet Seggie
South African Medical Journal

South African Medical Journal
Website: www.samj.org.za
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# ANNEXURE D: AUTHOR GUIDELINES FOR *HEALTH SA GESONDHEID*

The author guidelines for the journal Health SA Gesondheid are presented in this annexure exactly as it was given on http://www.elsevier.com/journals/health-sa-gesondheid/1025-9848/guide-for-authors#92000 on the 18th of August 2015.

Guide for Authors

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Strunk, W., Jr., & White, E. B. (2000). The elements of style. (4th ed.). New York: Longman, (Chapter 4).

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http://dx.doi.org/10.1016/j.physletb.2010.09.059

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# ANNEXURE E: AUTHOR GUIDELINES FOR THE *SOUTH AFRICAN MEDICAL JOURNAL*

The author guidelines for the second journal, the *South African Medical Journal*, are shown below as obtained from http://www.samj.org.za/index.php/samj/about/submissions#authorGuidelines on the 19th of September 2015.

## Author Guidelines

**Accepted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction, and will delay publication.**

### AUTHORSHIP

Named authors must consent to publication. Authorship should be based on: (i) substantial contribution to conception, design, analysis and interpretation of data; (ii) drafting or critical revision for important intellectual content; or (iii) approval of the version to be published. These conditions must all be met (uniform requirements for manuscripts submitted to biomedical journals; refer to **www.icmje.org**).

### CONFLICT OF INTEREST

Authors must declare all sources of support for the research and any association with a product or subject that may constitute conflict of interest.

### RESEARCH ETHICS COMMITTEE APPROVAL

Provide evidence of Research Ethics Committee approval of the research where relevant.

### PROTECTION OF PATIENT'S RIGHTS TO PRIVACY

Identifying information should not be published in written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) gives informed written consent for publication. The patient should be shown the manuscript to be published. Refer to **www.icmje.org**.

### ETHNIC CLASSIFICATION

References to ethnic classification must indicate the rationale for this.

**MANUSCRIPTS**

Shorter items are more likely to be accepted for publication, owing to space constraints and reader preferences.

***Research articles*** (previously 'Original articles') not exceeding 3 000 words, with up to 6 tables or illustrations, are usually observations or research of relevance to clinical medicine and related fields. *References should be limited to no more than 15.* Please provide a structured abstract not exceeding 250 words, with the following recommended headings: *Background, Objectives, Methods, Results,* and *Conclusion.*

***Scientific letters*** will be considered for publication as shorter ***Research articles***.

***Editorials***, Opinions, etc. should be about 1000 words and are welcome, but unless invited, will be subjected to the *SAMJ* peer review process.

***Review articles*** are rarely accepted unless invited.

***Letters to the editor***, for publication, should be about 400 words with only one illustration or table, and must include a correspondence address.

***Forum articles*** must be accompanied by a short description (50 words) of the affiliation details/interests of the author(s). Refer to recent forum articles for guidance. Please provide an accompanying abstract not exceeding 150 words.

***Book reviews*** should be about 400 words and must be accompanied by the publication details of the book.

***Obituaries*** should be about 400 words and may be accompanied by a photograph.

***Guidelines*** must be endorsed by an appropriate body prior to consideration and all conflicts of interest expressed. A structured abstract not exceeding 250 words (recommended sub-headings: *Background, Recommendations, Conclusion*) is required. Sections and sub-sections must be numbered consecutively (e.g. 1. Introduction; 1.1 Definitions; 2. etc.) and summarised in a Table of Contents. References, appendices, figures and tables must be kept to a minumum.

*Guidelines exceeding 8 000 words will only be considered for publication as a supplement to the* SAMJ*; the costs of which must be covered by sponsorship or advertising. The Editor reserves the right to determine the scheduling of supplements. Understandably, a delay in publication must be anticipated dependent upon editorial workflow.*

**MANUSCRIPT PREPARATION**

Refer to articles in recent issues for the presentation of headings and subheadings. If in doubt, refer to 'uniform requirements' - **www.icmje.org**. Manuscripts must be provided in **UK English**.

**Qualification, affiliation and contact details** of ALL authors must be provided in the manuscript and in the online submission process.

**Abbreviations** should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.

**Scientific measurements** must be expressed in SI units except: blood pressure (mmHg) and haemoglobin (g/dl). Litres is denoted with a lowercase 'l' e.g. 'ml' for millilitres). Units should be preceded by a space (except for %), e.g. '40 kg' and '20 cm' but '50%'. Greater/smaller than signs (> and 40 years of age'. The same applies to ± and º, i.e. '35±6' and '19ºC'.

**Numbers** should be written as grouped per thousand-units, i.e. 4 000, 22 160...

**Quotes** should be placed in single quotation marks: i.e. The respondent stated: '...' Round **brackets** (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.

**General formatting** The manuscript must be in Microsoft Word or RTF document format. Text must be single-spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes, with the exception of Tables).

**ILLUSTRATIONS AND TABLES**

If tables or illustrations submitted have been published elsewhere, the author(s) should provide consent to republication obtained from the copyright holder.

**Tables** may be embedded in the manuscript file or provided as **'supplementary files'**. They must be numbered in Arabic numerals (1,2,3...) and referred to consecutively in the text (e.g. 'Table 1'). Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged. Tables must be cell-based (i.e. not constructed with text boxes or tabs), and accompanied by a concise title and column headings. Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

**Figures** must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'. Figure legends: Fig. 1. 'Title...' All illustrations/figures/graphs must be of **high resolution/quality**: 300 dpi or more is preferable, but images must not be resized to increase resolution. Unformatted and uncompressed images must be attached individually as '**supplementary files**' upon submission (not solely embedded in the accompanying manuscript). TIFF and PNG formats are preferable; JPEG and PDF formats are accepted, but authors must be wary of image compression. Illustrations and graphs prepared in Microsoft Powerpoint or Excel must be accompanied by the original workbook.

**REFERENCES**

**References must be kept to a maximum of 15.** Authors must verify references from original sources. *Only complete, correctly formatted reference lists will be accepted.* Reference lists must be generated manually and **not** with the use of reference manager software. Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,[2] and others.[3,4-6]All references should be listed at the end of the article in numerical order of appearance in the **Vancouver style** (not alphabetical order). Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus. Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al. First and last page, volume and issue numbers should be given.

**Wherever possible, references must be accompanied by a digital object identifier (DOI) link and PubMed ID (PMID)/PubMed Central ID (PMCID).** Authors are encouraged to use the DOI lookup service offered by **CrossRef**.

**Journal references:** Price NC, Jacobs NN, Roberts DA, et al. Importance of asking about glaucoma. Stat Med 1998;289(1):350-355. [http://dx.doi.org/10.1000/hgjr.182] [PMID: 2764753]

**Book references:** Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975:96-101. *Chapter/section in a book:* Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA jun, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: WB Saunders, 1974:457-472.

**Internet references:** World Health Organization. The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Geneva: World Health Organization, 2002. http://www.who.int/whr/2002 (accessed 16 January 2010).

**Other references (e.g. reports)** should follow the same format: Author(s). Title. Publisher place: publisher name, year; pages. Cited manuscripts that have been accepted but not yet published can be included as references followed by '(in press)'. Unpublished observations and personal communications in the text must not appear in the reference list. The full name of the source person must be provided for personal communications e.g. '...(Prof. Michael Jones, personal communication)'.

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2. The submission has not been previously published, nor is it before another journal

for consideration.

3. The text complies with the stylistic and bibliographic requirements in **Author Guidelines**.

4. The manuscript is in Microsoft Word or RTF document format. The text is single-spaced, in 12-point Times New Roman font, and contains no unnecessary formatting.

5. Illustrations/figures are high resolution/quality (not compressed) and in an acceptable format (preferably TIFF or PNG). These must be submitted individually as 'supplementary files' (not solely embedded in the manuscript).

6. For illustrations/figures or tables that have been published elsewhere, the author has obtained written consent to republication from the copyright holder.

7. Where possible, references are accompanied by a digital object identifier (DOI) and PubMed ID (PMID)/PubMed Central ID (PMCID).

8. An abstract has been included where applicable.

9. The research was approved by a Research Ethics Committee (if applicable)

10. Any conflict of interest (or competing interests) is indicated by the author(s).

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# ANNEXURE F: INFORMED CONSENT FORMS AND QUESTIONNAIRES

This annexure contains, in the following order, the English informed consent form, the English questionnaire, the Afrikaans informed consent form, the Afrikaans questionnaire, the Setswana informed consent form and the Setswana questionnaire. To protect the identity of the participating tertiary academic institution, its name has been removed from these documents.


# PARTICIPANT INFORMATION LEAFLET FOR HOSTEL STUDENTS

**Version 3 (24 March 2015)**

## TITLE OF THE RESEARCH PROJECT:

**Self-reported use of methylphenidate by hostel students at a South African tertiary academic institution**

**REFERENCE NUMBER: NWU-00146-14-S1**

**PRINCIPAL INVESTIGATOR:**

Dr JR Burger

**ADDRESS:**

School of Pharmacy

North-West University

Private Bag X6001

Potchefstroom

2522

**CONTACT NUMBER:**

018 299 2285

You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the researcher any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Furthermore, your participation is **entirely voluntary** and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point prior to submitting the questionnaire, even if you do agree to take part.

**This study has been approved by the Health Research Ethics Committees at the North-West University and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research. It might be necessary for the research ethics committee members to inspect the research records.**

**Which criteria must I meet to participate in this study?**

- You must be a full-time contact student of [redacted]
- You must be 18 years old or older
- You must be affiliated with one of the ten chosen hostels
- You must understand either Afrikaans, English or Setswana

**What is this research study all about?**

- This study will be conducted at [redacted] and will involve a questionnaire.
- The objectives of this research are to investigate the use of methylphenidate (Ritalin®/ Concerta®) by students, for medical and nonmedical reasons, how students acquire methylphenidate and the students' knowledge of methylphenidate.
- Methylphenidate is a prescription stimulant used to treat Attention Deficit/ Hyperactivity Disorder or Attention Deficit Disorder (ADHD or ADD). All the students from ten randomly selected hostels (five sororities and five fraternities) will be asked to participate.

**Why have you been invited to participate?**

- You are being asked to participate in this study because your hostel has been selected to participate. We would like to know whether you have used methylphenidate, how you have used it if applicable and what you know about it. Your opinions and experiences are very valuable to us. In total, approximately 2000 students will be invited to participate.

**What will your responsibilities be?**

- If you agree to be in this study, you will be expected to complete a questionnaire, during which time you can share your opinions and experiences. The questionnaire should take approximately 20 minutes to complete. After completing the questionnaire, you can go to your Hostel Matron and throw the questionnaire and informed consent form into the locked and sealed box that we will provide. You may keep this information pamphlet. Please submit the questionnaire and informed consent form before 17:00 on Friday. You may withdraw from the study at any point after starting the questionnaire until you submit it. Since we cannot link the information you give to you, you will not be able to withdraw your data from the study after submitting.

**What are the researchers' responsibilities?**

- The researchers are responsible for ensuring that the research is carried in accordance with the research protocol, that your data remains anonymous and confidential, and finally to give you feedback on the results of the study should you ask for it.

**Will you benefit from taking part in this research?**

- There are no direct benefits to you as the participant. Your participation will however improve our understanding of the way, and reasons why students use methylphenidate. Therefore, the community will benefit from this study through the implementation of recommendations to encourage the safe use of methylphenidate.

**Are there risks involved in your taking part in this research?**

- The risk to you as a participant is minimal in this study. Filling in the questionnaire could cause you some emotional distress; however, you may rest assured that your answers are completely confidential. No personal information will be asked and your answers can by no means be traced back to you. Furthermore, should you be uncomfortable with answering any question, you may choose to skip it. Otherwise, you may also withdraw from the survey altogether.

**Who will have access to the data?**

- All data will be handled with strict confidentiality and will be stored on a password protected computer in a locked office. The only people who will work with the information you share will be the research team and a biostatistician consultant. No individual participants can be identified from the data he/she gave. As a result, participation is completely anonymous and no participant can be identified in any publication of the results.

**Who may inspect the research records?**

- The research records may be inspected by the Health Research Ethics Committee.

**Who are the members of the research team and what are their qualifications?**

- Project leader: Dr JR Burger (BPharm, MPharm, PhD)
- Researcher/ Post-graduate student: J Dreyer (BPharm)
- Co-supervisor: Mrs I Kotze (BPharm, MBA)
- Co-supervisor: Prof S van Dyk (BPharm, MSc, PhD)

**What will happen in the unlikely event of some form of discomfort occurring as a direct result of your taking part in this research study?**

- If a specific question makes you to uncomfortable, you may skip it and proceed to the next question. Alternatively, you may also withdraw from the study without any penalties. If you are concerned about the way you use methylphenidate or you are otherwise emotionally distressed, you can visit [redacted] at [redacted] or contact them at [redacted].

**Will you be paid to take part in this study and are there any costs involved?**

- No, you will not be paid to participate in this study and there will be no cost to you as a result of participation in this study.

**Is there anything else that you should know or do?**

- If you encounter any problems or have any questions regarding your consent or the survey, you are welcome to contact the project leader, Dr JR Burger at Johanita.Burger@nwu.ac.za or 018 299 2285.
- You are also welcome to contact the Health Research Ethics Committee of the Faculty of Health Sciences via Ms Carolien van Zyl at +27 18 299 2094 or Carolien.VanZyl@nwu.ac.za if you have any concerns or complaints that have not been adequately addressed by the researcher.
- You will receive a copy of this information and consent form for your own records.
- A presentation will be done at all the participating hostels regarding methylphenidate use, the dangers thereof and legal implications of its use.
- The findings of the research will be shared with the Student Dean who will relay the results to the hostel committees.
- The findings of the research will also be shared with you if you are interested. You are welcome to contact Dr JR Burger regarding this matter at Johanita.Burger@nwu.ac.za or 018 299 2285.

# INFORMED CONSENT FORM

## Declaration by participant

By signing below, I ……..…… agree to take part in a research study entitled: Self-reported use of methylphenidate by hostel students at a South African tertiary academic institution.

**I declare that:**

- I have read this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is voluntary and I have not been pressurised to take part.
- I may choose to leave the study at any time before submitting the questionnaire and will not be penalised or prejudiced in any way.

Signed at (*place*) .....…..…….. on (*date*) ……...……..2015.

..... .....

**Signature of participant** **Signature of witness**

## Declaration by person obtaining consent

I, (name)....., declare that:

- I explained the information in this document to (name).....
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above
- I did/did not use an interpreter.

Signed at (*place*) .....…..…….. on (*date*) ……...……..2015.

..... .....

**Signature of person obtaining consent** **Signature of witness**

## Declaration by researcher

I, J Dreyer, declare that:

- I explained the information in this document to (name).....
- I encouraged him/her to ask questions and took adequate time to answer them
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above
- I did not use an interpreter

Signed at (*place*) .....…..…….. on (*date*) ……...……...2015.

..... .....

Signature of researcher

# The Ritalin®/Concerta® study questionnaire

Thank you for taking this questionnaire!

The questionnaire has four sections. Section A is concerned with demographic information. Section B asks questions about how and why students use methylphenidate. Methylphenidate is a prescription stimulant that is used in the treatment of Attention-Deficit/Hyperactivity Disorder or Attention Deficit Disorder (ADHD or ADD). Sometimes, people also use methylphenidate for other reasons. The trade names for methylphenidate are Ritalin®, Ritalin LA®, Methylphenidate HCL Douglas® and Concerta®. Section C relates to where students get methylphenidate. The last section, Section D, relates to your perceptions of methylphenidate.

Please read each question and fill in the response that is most accurate for you. Give one response at each question unless otherwise instructed. Indicate your answer by making a cross in the blok. Your opinion is very valuable to us and therefore it is important to be as honest as possible.

The survey is completely voluntary. You may choose to withdraw at any stage before submitting the questionnaire and you may also choose to skip a question if you do not feel comfortable answering it.

Thank you for your time. Your participation is greatly appreciated!

# The Ritalin®/Concerta® study questionnaire

| Questionnaire number | |
|---|---|

SECTION A: Demographic questions

Please tell us about yourself.

(1) How old will you be at the end of 2015? ____ years

(2) In which academic year are you? ____ year

| (3) What is your gender? | |
|---|---|
| 1 | Male |
| 2 | Female |

| (4) In which faculty are you? | |
|---|---|
| 1 | Arts |
| 2 | Economic and Management Sciences |
| 3 | Education Sciences |
| 4 | Engineering |
| 5 | Health Sciences |
| 6 | Law |
| 7 | Natural Sciences |
| 8 | Theology |

SECTION B: Methylphenidate use

**Remember**:

Trade names for **methylphenidate** are: Ritalin®, Ritalin LA®, Methylphenidate HCL Douglas® and Concerta®.

**Healthcare practitioner** is a person who is qualified to diagnose Attention-Deficit/Hyperactivity Disorder or Attention Deficit Disorder (ADHD or ADD); for example a general practitioner, psychiatrist, paediatrician, etc.

**Medical purpose means** using the drug for the reason the prescriber said you need it. For example using methylphenidate for diagnosed ADHD. .

**Nonmedical purpose means** using the drug for other reasons than what it was prescribed for, such as staying awake and partying.

**Prescriber** is a doctor (for example a general practitioner, psychiatrist, paediatrician, etc.) who may prescribe medicine

**Prescription** is the document written by a prescriber, to a pharmacist, which contains instructions for the dispensing of medication.

| (5) | Has a healthcare practitioner EVER officially diagnosed you with Attention-Deficit/Hyperactivity Disorder or Attention Deficit Disorder (ADHD or ADD)? |
|---|---|
| 1 | Yes |
| 2 | No |
| 3 | I do not know |

| (6) | Have you EVER used methylphenidate? |
|---|---|
| 1 | Yes |
| 2 | No |

| (7) | When was the first time you used methylphenidate? |
|---|---|
| 1 | Before primary school |
| 2 | Primary school |
| 3 | High school |
| 4 | University |
| 5 | Other, *please specify*_____ |
| 6 | *I have never used methylphenidate* |

| (8) | Have you used methylphenidate during your time at university? |
|---|---|
| 1 | Yes |
| 2 | No |

| (9) | How often have you had a **prescription** for the methylphenidate you have used? |
|---|---|
| 1 | Always |
| 2 | Usually |
| 3 | Sometimes |
| 4 | Rarely |
| 5 | Never |
| 6 | *I have never used methylphenidate* |

(10) How often have you used your **prescribed** methylphenidate? Tick the most appropriate block for each row. If you have never been prescribed methylphenidate please tick the last column.

| | **Always** | **Usually** | **Sometimes** | **Rarely** | **Never** | ***I have never been prescribed methylphenidate*** |
|---|---|---|---|---|---|---|
| In **excess** of what was **prescribed** to you? | | | | | | |
| For **nonmedical** purposes (for another reason than that given by the prescriber, e.g. to stay awake, or partying, etc.) | | | | | | |

| (11) | How often do you usually use methylphenidate? *Tick all the blocks that are relevant for you.* |
|---|---|
| 1 | Every day |
| 2 | Weekends |
| 3 | Before class tests |
| 4 | Before semester tests |
| 5 | Before exams |
| 6 | *I have never used methylphenidate* |

(12) IF you have EVER used methylphenidate, **why did you do so**? *Tick all the blocks that are relevant to you*.

| | **Always** | **Usually** | **Sometimes** | **Rarely** | **Never** | ***I have never used methylphenidate*** |
|---|---|---|---|---|---|---|
| To study | | | | | | |
| To get high | | | | | | |
| To improve concentration | | | | | | |
| To party | | | | | | |
| To lose weight | | | | | | |
| To exercise better | | | | | | |
| Peer pressure | | | | | | |
| For my ADHD or ADD | | | | | | |
| Other, *please specify*_____ _____ | | | | | | |

(13) Which **products** do you use and how much would you typically use in one day? Tick all the blocks that are relevant to you. Say which products you have used and fill in the total number of tablets you typically take in one day.

| Tick | Product | Number of tablets per day |
|---|---|---|
| | Ritalin 10mg® | ___ tablets per day |
| | Ritalin LA 20mg® | ___ tablets per day |
| | Ritalin LA 30mg® | ___ tablets per day |
| | Ritalin LA 40mg® | ___ tablets per day |
| | Methylphenidate HCL Douglas 10mg® | ___ tablets per day |
| | Concerta 18mg® | ___ tablets per day |
| | Concerta 27mg® | ___ tablets per day |
| | Concerta 36mg® | ___ tablets per day |
| | Concerta 54mg® | ___ tablets per day |
| | I don't know what product I use | |
| | *I have never used methylphenidate* | |

(14) How do you take the product(s) that you use/have used? *Tick all the blocks that are relevant for you.*

| Product | Swallow | Snort | Inject | Other ***(please say how)*** |
|---|---|---|---|---|
| Ritalin 10mg® | | | | |
| Ritalin LA 20mg® | | | | |
| Ritalin LA 30mg® | | | | |
| Ritalin LA 40mg® | | | | |
| Methylphenidate HCL Douglas 10mg® | | | | |
| Concerta 18mg® | | | | |
| Concerta 27mg® | | | | |
| Concerta 36mg® | | | | |
| Concerta 54mg® | | | | |
| I do not know what product I use | | | | |
| *I have never used methylphenidate* | | | | |

SECTION C: Obtaining methylphenidate

(15) How often have you gotten your methylphenidate from? *Tick all the blocks that are relevant for you*.

| | **Always** | **Usually** | **Sometimes** | **Rarely** | **Never** | ***I have never used methylphenidate*** |
|---|---|---|---|---|---|---|
| A pharmacy **with a prescription** written by a **prescriber** | | | | | | |
| A pharmacy **with a <u>fake prescription</u>** | | | | | | |
| A pharmacy **without a prescription** | | | | | | |
| Friends | | | | | | |
| Family | | | | | | |
| The Internet | | | | | | |
| Other, *please specify*_____ | | | | | | |

(16) **If you wanted to**, do you think you could get methylphenidate from? Select 'Yes' to all that are true for you and 'No' to all that are false for you.

| **Yes** | **No** | |
|---|---|---|
| | | A pharmacy **with a prescription** written by a **prescriber** |
| | | A pharmacy **with a <u>fake prescription</u>** |
| | | A pharmacy **without a prescription** |
| | | Friends |
| | | Family |
| | | The internet |
| | | Other, *please specify*_____ |

*For the next set of questions, please rate how much you agree or disagree with the following statements.*

| | | **Strongly disagree** | **Disagree** | **I do not know** | **Agree** | **Strongly agree** |
|---|---|---|---|---|---|---|
| (17) | It is very easy to get hold of methylphenidate | | | | | |
| (18) | It is easy to find a prescriber (e.g. doctor) to write a prescription for methylphenidate, even if a student does not really have ADD/ADHD. | | | | | |

SECTION D: Your opinion of methylphenidate

(19) As far as you know, how often have you experienced the following because of using methylphenidate? *Tick all the blocks that are relevant to you*.

| | **Always** | **Usually** | **Sometimes** | **Rarely** | **Never** | ***I have never used methylphenidate*** |
|---|---|---|---|---|---|---|
| Headache | | | | | | |
| Stomach ache | | | | | | |
| Irritation | | | | | | |
| Reduced appetite | | | | | | |
| Sleep difficulties | | | | | | |
| Dizziness | | | | | | |
| Heart racing | | | | | | |
| Nervousness | | | | | | |
| Anger | | | | | | |
| Other, *please specify*_____ | | | | | | |

*For the next set of questions, please say whether you think each statement is true or false.*

| | | **True** | **False** | **I do not know** |
|---|---|---|---|---|
| (20) | Using methylphenidate without a prescription is illegal | | | |
| (21) | Methylphenidate can be used to build muscle | | | |
| (22) | Methylphenidate can make you hungry | | | |
| (23) | Methylphenidate can make you sleepy | | | |

The survey is now complete! Remember that you cannot withdraw your data after handing in your questionnaire at the hostel matron, since we cannot trace your data back to you.

Thank you for your time and participation!


# DEELNEMERINLIGTINGSTUK VIR KOSHUISSTUDENTE

**Weergawe 3 (24 Maart 2015)**

## TITEL VAN DIE NAVORSINGSPROJEK:

**Self-gerapporteerde metielfenidaat gebruik deur koshuisstudente by ’n Suid-Afrikaanse tersiêre akademiese instelling**

**VERWYSINGSNOMMER: NWU-00146-14-S1**

**HOOFNAVORSER:**

Dr JR Burger

**ADRES:**

Skool vir Farmasie

Noordwes-Universiteit

Privaatsak X6001

Potchefstroom

2522

**KONTAKNOMMER:**

018 299 2285

U word hiermee vriendelik uitgenooi om aan die bogenoemde navorsingprojek deel te neem. Neem asseblief ŉ oomblik om die volgende inligtingsblad te lees wat die besonderhede van die projek bevat. Vra gerus enige vrae rakende enige deel van die projek wat u nie heeltemal verstaan nie aan die navorser. Dit is baie belangrik dat u duidelik verstaan wat die navorsing behels en hoe u kan deelneem. U deelname is **heeltemal vrywillig** en u is welkom om deelname te weier. As u weier, sal dit u op geen manier negatief affekteer nie. Selfs al stem u in om deel te neem aan die studie, kan u steeds ter enige tyd voor die vraelys ingedien is van die studie onttrek.

**Hierdie studie is deur die Gesondheidsnavorsing-Etiekkomitee van die Noordwes-Universiteit goedgekeur en sal uitgevoer word volgens die etiese riglyne en beginsels van die internasionale Verklaring van Helsinki, Suid-Afrikaanse Riglyne vir Goeie Kliniese Praktyk en die Mediese Navorsingsraad Etiese Riglyne vir Navorsing. Dit mag dalk nodig wees vir die navorsings-etiekkomiteelede om die navorsingsdata te inspekteer.**

**Aan watter kriteria moet ek voldoen om deel te neem aan hierdie studie?**

- U moet ŉ voltydse kontakstudent van [redacted] wees;
- U moet 18 jaar of ouer wees;
- U moet ŉ inwoner van een van die 10 verkose koshuise wees; en
- U moet Afrikaans, Engels of Setswana kan verstaan.

**Waaroor gaan hierdie studie?**

- Hierdie studie sal uitgevoer word by [redacted] en behels ŉ vraelys.
- Die doelwitte van die studie is om die gebruik van metielfenidaat (Ritalin®/ Concerta®) deur studente vir mediese en nie-mediese redes, hoe studente metielfenidaat bekom, en wat studente weet van metielfenidaat, te ondersoek.
- Metielfenidaat is ŉ voorskrifstimulant wat gebruik word om aandagsgebreksindroom te behandel. Al die studente van die tien lukraakverkose koshuise (vyf dames-, en vyf manskoshuise) sal genooi word om deel te neem.

**Hoekom is ek uitgenooi om deel te neem?**

- U word uitgenooi om deel te neem omdat u koshuis as deel van die projek gekies is. Ons wil graag uitvind of u al ooit metielfenidaat gebruik het, en indien dit van toepassing is, hoe u dit bekom het, en wat u daarvan weet. U opinies en ervaringe is baie belangrik vir ons. Ongeveer 2 000 studente word genooi om deel te neem.

**Wat sal my verantwoordelikhede wees?**

- As u instem om aan die studie deel te neem, sal daar van u verwag word om ŉ vraelys te voltooi waar u die geleentheid sal kry om u opinies en ervarings te deel. Die vraelys sal ongeveer 20 minute neem om te voltooi. Nadat u die vraelys voltooi het, kan u na die Koshuistannie toe gaan en die vraelys en ingeligte toestemmingsvorm in die geslote, verseëlde boks wat die navorsers sal verskaf, gooi. U mag hierdie inligtingstuk hou. Handig asseblief die vraelys en ingeligte kennisvorm teen 17:00 op Vrydagmiddag in. U mag uit die studie onttrek van enige punt nadat u die vraelys begin totdat u die vraelys ingee. Aangesien ons nie die inligting wat u gee aan u identiteit kan verbind nie, sal u nie die inligting kan onttrek nadat u die vraelys ingehandig het nie.

**Wat is die navorsers se verantwoordelikhede?**

- Die navorsers is verantwoordelik daarvoor om seker te maak dat die navorsing in ooreenstemming met die navorsingsprotokol uitgevoer word, dat die data anoniem en vertroulik bly, en laastens om aan u terugvoer oor die studie te gee indien u daarvoor vra.

**Sal ek bevoordeel word deur deel te neem aan die studie?**

- Daar is geen direkte voordele aan u as die deelnemer nie. U deelname sal wel ons begrip van die manier wat studente metielfenidaat gebruik, en hoekom studente dit gebruik, verbeter. Dus sal die gemeenskap by die studie baat vind aangesien dit kan lei tot die implementering van voorstelle om die veilige gebruik van metielfenidaat aan te moedig.

**Is daar enige risiko's verbonde aan my deelname in die studie?**

- Die risiko vir u as deelnemer in die studie is minimaal. Deur die vraelys in te vul, mag u dalk ongemaklik of ontsteld voel, maar u kan verseker wees dat u antwoorde heeltemal vertroulik is. Ons vra nie vir enige persoonlike inligting nie, so u antwoorde kan glad nie aan u gekoppel word nie. Verder kan u kies om 'n vraag oor te slaan indien u nie gemaklik voel om dit te beantwoord nie. Andersins mag u ook heeltemal uit die studie onttrek, indien u so voel.

**Wie sal toegang tot die data hê?**

- Alle data sal met streng vertroulikheid behandel word en sal gestoor word op 'n wagwoord-beskermende rekenaar in 'n geslote kantoor. Die enigste mense wie met u inligting sal werk, sal die navorsingspan en 'n konsulterende biostatistikus wees. Geen individuele deelnemer kan deur die data wat hy/sy verskaf geïdentifiseer word nie. As gevolg daarvan is deelname heeltemal anoniem en geen deelnemer kan in enige publikasie van die resultate geïdentifiseer word nie.

**Wie mag die navorsingsdokumente inspekteer?**

- Die navorsingsdokumente mag deur die Gesondheidsnavorsing-etiekkomitee geïnspekteer word.

**Wie is die lede van die navorsingspan en wat is hul kwalifikasies?**

- Projekleier: Dr JR Burger (BPharm, MPharm, PhD)
- Navorser/Nagraadse student: Mej J Dreyer (BPharm)
- Medestudieleier: Mev I Kotze (BPharm, MBA)
- Hulpstudieleier: Prof S van Dyk (BPharm, MSc, PhD)

**Wat sal gebeur in die onwaarskynlike geval dat ek emosionele onrus beleef as 'n direkte gevolg van my deelname aan die studie?**

- As 'n spesifieke vraag u ongemaklik laat voel mag u dit oorslaan en aangaan na die volgende vraag. Andersins mag u ook uit die studie onttrek sonder enige nagevolge. As u bekommerd is oor die manier waarop u metielfenidaat gebruik, of u is andersins ontsteld, mag u [redacted] by [redacted] besoek, of hulle kontak by [redacted].

**Sal ek betaal word om deel te neem aan hierdie studie en is daar enige kostes daaraan verbonde?**

- Nee, u sal geen vergoeding ontvang vir deelname aan hierdie studie nie en daar is geen koste daaraan verbonde as gevolg van u deelname aan die studie nie.

**Is daar enige-iets anders wat ek moet weet of doen?**

- As u enige probleme ondervind of enige vrae het rakende u toestemming of die vraelys is u welkom om die projekleier, Dr JR Burger by Johanita.Burger@nwu.ac.za of 018 299 2285 te kontak.
- U kan ook gerus die Gesondheidnavorsing-etiekkomitee van die Fakulteit Gesondheidswetenskap nader deur mej Carolien van Zyl te skakel by +27 18 299 2094 of te kontak by Carolien.VanZyl@nwu.ac.za as u enige bekommernisse of klagtes het wat nie behoorlik deur die navorsers aangespreek is nie.
- U sal 'n afskrif van hierdie inligting en die toestemmingsvorm vir u eie rekords ontvang.
- Daar sal 'n aanbieding gelewer word by al die deelnemende koshuise rakende metielfenidaatgebruik, die gevare daarvan en die wetlike implikasies van die gebruik daarvan.
- Die bevindinge van die navorsing sal met die Studentedekaan gedeel word, wie die resultate aan die koshuisraad sal oorgee.
- Sou u belangstel, sal die resultate van die studie ook met u gedeel word. U is welkom om dr JR Burger hieroor te skakel by Johanita.Burger@nwu.ac.za of 018 299 2285.

# INGELIGTE TOESTEMMINGSVORM

## Verklaring deur die deelnemer

Deur onder te teken, stem ek, ……. in om deel te neem aan die navorsingsprojek getiteld: Self-gerapporteerde gebruik van metielfenidaat deur koshuisstudente by 'n Suid-Afrikaanse tersiêre akademiese instelling.

**Ek verklaar dat:**

- Ek die inligtingstuk en ingeligte toestemmingsvorm gelees het en dat dit geskryf is in 'n taal waarin ek vlot is en mee gemaklik voel.
- Ek kans gehad het om vrae te vra en al my vrae voldoende beantwoord is.
- Ek verstaan dat deelname aan die studie vrywillig is en dat ek nie onder druk geplaas was om deel te neem nie.
- Ek kan kies om uit die studie te onttrek op enige stadium totdat ek die vraelys inhandig het, en sal nie benadeel of bevooroordeel word as gevolg daarvan nie.

Geteken te (*plek*) .....…..…….. op (*datum*) ……...……..2015.

..... .....

**Handtekening van die deelnemer** **Handtekening van getuie**

## Verklaring deur die persoon wie toestemming verkry

Ek, (naam)....., verklaar dat:

- Ek die inligting in hierdie dokument aan (naam)..... verduidelik het.
- Ek het hom/haar aangemoedig om vrae te vra en dat ek genoeg tyd spandeer het om daardie vrae te beantwoord.
- Ek is tevrede dat hy/sy alle aspekte van die studie, soos bo bespreek, verstaan.
- Ek nie gebruik gemaak het van 'n tolk nie.

Geteken te (*plek*) .....…..…….. op (*datum*) ……...……..2015.

..... .....

**Handtekening van persoon wie toestemming verkry** **Handtekening van getuie**

## Verklaring deur die navorser

Ek, J Dreyer, verklaar dat:

- Ek die inligting in hierdie dokument aan (naam)..... verduidelik het.
- Ek het hom/haar aangemoedig om vrae te vra en dat ek genoeg tyd spandeer het om daardie vrae te beantwoord.
- Ek tevrede is dat hy/sy alle aspekte van die studie, soos bo bespreek, verstaan.
- Ek nie gebruik gemaak het van ’n tolk nie.

Geteken by (*plek*) .....…..…….. op (*datum*) ……...……..2015.

..... .....

**Handtekening van navorser** **Handtekening van getuie**

# Die Ritalin®/Concerta®-studievraelys

Dankie vir u deelname!

Die vraelys bestaan uit vier afdelings. Afdeling A hanteer demografiese inligting. Afdeling B vra vrae oor hoe en waarom studente metielfenidaat gebruik. Metielfenidaat is ’n voorskrifstimulant wat gebruik word in die behandeling van aandagsgebreksindroom (ADHD of ADD). Soms gebruik mense dit ook vir ander redes. Handelsname van metielfenidaat is Ritalin®, Ritalin LA®, Methylphenidate HCL Douglas® en Concerta®. Afdeling C handel oor waar studente metielfenidaat bekom. Die laaste afdeling, Afdeling D, handel oor u persepsies rakende metielfenidaat.

Lees asseblief elke vraag noukeurig deur en vul die antwoord wat die akkuraatste vir u is, in. Gee slegs een antwoord by elke vraag, behalwe as u gevra word vir meer as een antwoord. Dui u antwoord aan deur ’n kruis in die blokkie te maak. U opinie is baie waardevol vir ons en dus is dit belangrik dat u so eerlik as moontlik is.

Deelname aan die studie is heeltemal vrywillig. U mag kies om uit die studie te onttrek voordat die vraelys ingehandig word en u mag kies om ’n vraag oor te slaan as u nie gemaklik voel met die vraag nie.

Dankie vir u tyd. U deelname word opreg waardeer!

# Die Ritalin®/Concerta®-studievraelys

| Vraelys nommer | |
|---|---|

AFDELING A: Demografiese vrae

Vertel ons asseblief van uself.

(1) Hoe oud sal u wees aan die einde van 2015? ____ jaar oud

(2) In watter akademiese jaar is u? ____ jaar

| (3) | Dui asseblief u geslag aan. |
|---|---|
| 1 | Manlik |
| 2 | Vroulik |

| (4) | In watter fakulteit studeer u? |
|---|---|
| 1 | Lettere en Wysbegeerte |
| 2 | Ekonomiese en Bestuurswetenskappe |
| 3 | Opvoedingswetenskappe |
| 4 | Ingenieurswese |
| 5 | Gesondheidswetenskappe |
| 6 | Regte |
| 7 | Natuurwetenskappe |
| 8 | Teologie |

AFDELING B: Metielfenidaat gebruik

**Let wel**:

Handelsname vir **metielfenidaat** is: Ritalin®, Ritalin LA®, Methylphenidate HCL Douglas® en Concerta®.

'n **Gesondheidsorgpraktisyn** is 'n persoon wie gekwalifiseer is om aandagsgebreksindroom (ADHD of ADD) te diagnoseer; byvoorbeeld 'n familiedokter, psigiater, pediater, ens.

**Mediese gebruik beteken** om die middel te gebruik vir die rede waarvoor die geneesheer dit voorgeskryf het, byvoorbeeld om metielfenidaat te gebruik vir gediagnoseerde ADHD.

**Nie-mediese gebruik beteken** om die middel te gebruik vir ander redes as waarvoor die produk voorgeskryf was, byvoorbeeld om wakker te bly of partytjie te hou.

**Voorskrywer** is 'n dokter (byvoorbeeld 'n familiedokter, psigiater, pediater, ens.) wie gemagtig is om die medisyne voor te skryf.

'n **Voorskrif** is 'n dokument wat deur 'n voorskrywer geskryf is, aan 'n apteker, wat instruksies rakende die reseptering van medikasie gee.

| (5) | Het 'n gesondheidsorgpraktisyn u al OOIT amptelik met aandagsgebreksindroom (ADHD of ADD) gediagnoseer? |
|---|---|
| 1 | Ja |
| 2 | Nee |
| 3 | Ek weet nie |

| (6) | Het u al OOIT metielfenidaat gebruik? |
|---|---|
| 1 | Ja |
| 2 | Nee |

| (7) | Wanneer het u metielfenidaat vir die eerste keer gebruik? |
|---|---|
| 1 | Voor laerskool |
| 2 | Laerskool |
| 3 | Hoërskool |
| 4 | Universiteit |
| 5 | Ander, *spesifiseer asseblief*_____ |
| 6 | *Ek het nog nooit metielfenidaat gebruik nie* |

| (8) | Het u al metielfenidaat tydens u tyd by die universiteit gebruik? |
|---|---|
| 1 | Ja |
| 2 | Nee |

| (9) | Hoe gereeld het u ’n **voorskrif** vir die metielfenidaat wat u gebruik het, bekom? |
|---|---|
| 1 | Altyd |
| 2 | Gewoonlik |
| 3 | Partykeer |
| 4 | Selde |
| 5 | Nooit |
| 6 | *Ek het nog nooit metielfenidaat gebruik nie* |

(10) Hoe gereeld het u al u **voorgeskrewe** metielfenidaat? Maak ’n kruis in die geskikte blokkie van elke ry. As u nog nooit ’n voorskrif vir metielfenidaat gehad het nie, merk die laaste kolom.

| | **Altyd** | **Gewoonlik** | **Partykeer** | **Selde** | **Nooit** | ***Metielfenidaat was nog nooit aan my voorgeskryf nie*** |
|---|---|---|---|---|---|---|
| In **oormaat** gebruik as wat **voorgeskryf** was aan u? | | | | | | |
| Gebruik vir **nie-mediese** redes (vir enige rede behalwe die rede hoekom die voorskrywer dit voorgeskryf het, bv. om wakker te bly, of partytjie te hou, ens.) | | | | | | |

| (11) | Hoe gereeld gebruik u gewoonlik metielfenidaat? *Merk al die blokkies wat op u van toepassing is.* |
|---|---|
| 1 | Elke dag |
| 2 | Naweke |
| 3 | Voor klastoetse |
| 4 | Voor semestertoetse |
| 5 | Voor eksamens |
| 6 | *Ek het nog nooit metielfenidaat gebruik nie* |

(12) AS u al OOIT metielfenidaat gebruik het, **hoekom het u dit gebruik**? *Merk al die blokkies wat op u van toepassing is.*

| | **Altyd** | **Gewoonlik** | **Partykeer** | **Selde** | **Nooit** | ***Ek het nog nooit metielfenidaat gebruik nie*** |
|---|---|---|---|---|---|---|
| Om te leer/studeer | | | | | | |
| Om hoog te word | | | | | | |
| Om my konsentrasie te verbeter | | | | | | |
| Om partytjie te hou | | | | | | |
| Om gewig te verloor | | | | | | |
| Om beter te oefen | | | | | | |
| Groepsdruk | | | | | | |
| Vir my ADHD of ADD | | | | | | |
| Ander, *spesifiseer asseblief*_____ _____ | | | | | | |

(13) Watter **produkte** gebruik u en hoeveel sal u tipies op een dag gebruik? Merk al die blokkies wat op u van toepassing is. Sê watter produkte u al gebruik het en vul die totale hoeveelheid tablette wat u tipies op een dag sal neem, in.

| **Merk** | **Produk** | **Hoeveelheid tablette per dag** |
|---|---|---|
| | Ritalin 10mg® | ___ tablette per dag |
| | Ritalin LA 20mg® | ___ tablette per dag |
| | Ritalin LA 30mg® | ___ tablette per dag |
| | Ritalin LA 40mg® | ___ tablette per dag |
| | Methylphenidate HCL Douglas 10mg® | ___ tablette per dag |
| | Concerta 18mg® | ___ tablette per dag |
| | Concerta 27mg® | ___ tablette per dag |
| | Concerta 36mg® | ___ tablette per dag |
| | Concerta 54mg® | ___ tablette per dag |
| | *Ek weet nie watter produk ek gebruik nie* | |
| | *Ek het nog nooit metielfenidaat gebruik nie* | |

(14) Hoe neem u die produk(te) wat u al gebruik het? *Merk al die blokkies wat op u van toepassing is.*

| **Produk** | **Sluk** | **Snuif** | **Inspuit** | **Ander *(dui asseblief aan hoe)*** |
|---|---|---|---|---|
| Ritalin 10mg® | | | | |
| Ritalin LA 20mg® | | | | |
| Ritalin LA 30mg® | | | | |
| Ritalin LA 40mg® | | | | |
| Methylphenidate HCL Douglas 10mg® | | | | |
| Concerta 18mg® | | | | |
| Concerta 27mg® | | | | |
| Concerta 36mg® | | | | |
| Concerta 54mg® | | | | |
| *Ek weet nie watter produk ek gebruik nie* | | | | |
| *Ek het nog nooit metielfenidaat gebruik nie* | | | | |

AFDELING C: Verkryging van metielfenidaat

(15) Hoe dikwels het u al u metielfenidaat verkry van? *Merk al die blokkies wat op u van toepassing is.*

| | **Altyd** | **Gewoonlik** | **Partykeer** | **Selde** | **Nooit** | ***Ek het nog nooit metielfenidaat gebruik nie*** |
|---|---|---|---|---|---|---|
| ŉ Apteek, **met ŉ voorskrif** wat deur ŉ **voorskrywer** voorgeskryf is | | | | | | |
| ŉ Apteek, **met ŉ vervalsde voorskrif** | | | | | | |
| ŉ Apteek, **sonder ŉ voorskrif** | | | | | | |
| Vriende | | | | | | |
| Familie | | | | | | |
| Die Internet | | | | | | |
| Ander, *spesifiseer asseblief*_____ | | | | | | |

(16) **As u sou wou,** dink u, u sal metielfenidaat kan kry by? Merk 'Ja' by elke stelling wat waar is vir u en 'Nee' by elke stelling wat vals is vir u.

| **Ja** | **Nee** | |
|---|---|---|
| | | ŉ Apteek, **met ŉ voorskrif** wat deur ŉ **voorskrywer** voorgeskryf is |
| | | ŉ Apteek, **met ŉ vervalsde voorskrif** |
| | | ŉ Apteek, **sonder ŉ voorskrif** |
| | | Vriende |
| | | Familie |
| | | Die Internet |
| | | Ander, *spesifiseer asseblief*_____ |

*By die volgende stel vrae, dui asseblief aan tot watter mate u saam stem, of nie saam stem nie met die volgende stellings.*

| | | **Stem glad nie saam nie** | **Stem nie saam nie** | **Ek weet nie** | **Stem saam** | **Stem sterk saam** |
|---|---|---|---|---|---|---|
| (17) | Dit is baie maklik om metielfenidaat in die hande te kry | | | | | |
| (18) | Dit is maklik om 'n voorskrywer (bv. 'n dokter) te kry wie 'n voorskrif vir metielfenidaat sal skryf, al het die student nie aandagsgebreksindroom (ADD/ADHD) nie. | | | | | |

AFDELING D: U opinie oor metielfenidaat

(19) Sover u weet, hoe gereeld het u al die volgende as gevolg van die gebruik van metielfenidaat ervaar ? *Merk al die blokkies wat op u van toepassing is.*

| | **Altyd** | **Gewoonlik** | **Partykeer** | **Selde** | **Nooit** | ***Ek het nog nooit metielfenidaat gebruik nie*** |
|---|---|---|---|---|---|---|
| Hoofpyn | | | | | | |
| Maagpyn | | | | | | |
| Irritasie | | | | | | |
| Verminderde eetlus | | | | | | |
| Slaapversteurings | | | | | | |
| Duiseligheid | | | | | | |
| Hart wat vinnig klop | | | | | | |
| Senuweeagtigheid | | | | | | |
| Woede | | | | | | |
| Ander, *spesifiseer asseblief*_____ | | | | | | |

*Dui by die volgende stel vrae asseblief aan of u dink die stellings is waar of vals.*

| | | **Waar** | **Vals** | **Ek weet nie** |
|---|---|---|---|---|
| (20) | Dit is onwettig om metielfenidaat sonder ’n voorskrif te gebruik | | | |
| (21) | Metielfenidaat kan gebruik word om spiere te bou | | | |
| (22) | Metielfenidaat kan jou honger maak | | | |
| (23) | Metielfenidaat kan jou lomerig maak | | | |

Die vraelys is nou voltooi! Onthou dat u nie u data kan onttrek nadat u die vraelys in die boks by die Koshuistannie gegooi het nie, omdat ons nie u data aan u kan koppel nie.

Dankie vir u tyd en deelname!


# PAMPITSHANA YA TSHEDIMOSETSO YA MOTSAYAKAROLO GO BAITHUTI BA HOSETELE

**Tokololo 3 (24 Mopitlwe 2015)**

## SETLHOGO SA POROJEKE YA PATLISISO:

**Go ipega ga baithuti ba hosetele gore ba dirisa methylphenidate kwa setheong sa akatemi sa thešiari ya Aforikaborwa**

**NOMORETSHUPETSO: NWU-00146-14-S1**

**MMATLISISI-MOGOLO:**

Ngaka JR Burger

**ATERESE:**

Sekolo sa Khemisi

Yunibesiti ya Bokone-Bophirima

Private Bag X6001

Potchefstroom

2522

**DINOMORE TSA GO IKGOLAGANYA LE ENE:**

018 299 2285

O kopiwa go tsaya karoolo mo porojekeng ya patlisiso. Tsweetswee iphe nako ya go buisa tshedimosetso e e fano, e e tla tlhalosang dintlha tsa porojeke eno. Tsweetswee botsa mmatlisisi dipotso dipe fela ka karolo epe fela e o sa e tlhaloganyeng ka botlalo ya porojeke eno. Go botlhokwa gore o kgotsofale ka botlalo gore o tlhaloganya sentle gore ke eng se se tlileng go dirwa mo patlisisong eno le gore o ka tsaya karolo jang. Mo godimo ga moo, go tsaya karolo gago ke ga **boithaopo gotlhelele** e bile o gololesegile go gana go tsaya karolo. Fa o gana go tsaya karolo, seno ga se kitla se go ama le fa e le ka tsela epe e e sa siamang. Gape o gololesegile go ikgogela morago mo patlisisong nako nngwe le nngwe pele o re naya pampiri eno ya dipotso tsa go patlisiso, le fa o dumela go tsaya karolo.

**Patlisiso eno e rebotswe ke Dikomiti tsa Maitshwaro a a Siameng tsa Patlisiso kwa Yunibesiting ya Bokone-Bophirima mme e tla dirwa go ya ka dikaelo tsa maitshwaro a a siameng le melaometheo ya Maikano a Boditšhabatšhaba a Helsinki, Dikaelo tsa Aforika Borwa tsa Tlwaelo e e Molemo ya tsa Kalafi le Dikaelo tsa Maitshwaro a a Siameng tsa Patlisiso tsa Lekgotla la Patlisiso ka tsa Kakafi kgotsa Medical Research Council (MRC). Go ka nna ga tlhokega gore maloko a komiti ya patlisiso ya maitshwaro a a siameng a tlhatlhobe direkoto tsa patlisiso.**

**Ke tshwanetse go fitlhelela ditlhokego dife gore ke tseye karolo mo patlisisong eno?**

- O tshwanetse o bo o le moithuti wa nako e e tletseng yo o ithutelang mo setheong sa thuto [redacted]
- O tshwanetse go bo o le dingwaga di le 18 kgotsa go feta
- O tshwanetse go bo o le leloko la nngwe ya dihosetele di le some tse di tlhophilweng
- O tshwanetse go bo o tlhaloganya Aforikanse, Seesemane kgotsa Setswana

**Thuto-patlisiso eno e ka ga eng?**

- Patlisiso eno e tla direlwa [redacted] mme e tla dirisa pampiri ya dipotso tsa patlisiso.
- Maikaelelo a patlisiso eno ke go dira patlisiso ka ga tiriso ya methylphenidate (Ritalin®/ Concerta®) ke baithuti, ka mabaka a tsa kalafi le a e seng a tsa kalafi, gore baithuti ba e tsere kae le gore baithuti ba itse eng ka methylphenidate.
- Methylphenidate ke setlhare se se tlhagafatsang motho se motho a se newang ke ngaka se se dirisediwang go alafa Go sa kgone go tlhoma mogopolo/ Bothata jwa Matlhagatlhaga a a Feteletseng kgotsa Bothata jwa go sa kgone go Tlhoma Mogopolo, e leng Attention Deficit/ Hyperactivity Disorder or Attention Deficit Disorder (ADHD kgotsa ADD). Baithuti botlhe go tswa kwa dihoseteleng tse di tlhophilweng go sa latelwe thulaganyo e e rileng (tse tlhano tsa basadi le tse tlhano tsa banna) di tla kopiwa go tsaya karolo.

**Goreng o kopilwe go tsaya karolo?**

- O kopiwa go tsaya karolo mo patlisisong eno ka gonne hosetele ya gago e tlhophilwe gore e tseye karolo. Re batla go itse gore a o kile wa dirisa methylphenidate, o e dirisitse jang fa e le gore o kile wa e dirisa le gore o itse eng ka yone. Dikgopolo le maitemogelo a gago di botlhokwa thata mo go rona. Go tla kopiwa mo e ka nnang palogotlhe ya baithuti ba le 2000 gore ba tseye karolo.

**Maikarabelo a gago e tla nna afe?**

- Fa o dumela go tsenela patlisiso eno, go tla lebelelwa gore o tlatse pampiri ya dipotso tsa patlisiso, ka nako e o ka re nayang dikgopolo le maitemogelo a gago. Pampiri ya dipotso tsa patlisiso e tshwanetse go tsaya metsotso e le 20 go e tlatsa. Fa o sena go tlatsa pampiri ya dipotso tsa patlisiso, o ka nna wa ya kwa Meiteroneng wa Hosetele ya lona go ya go latlhela pampiri ya dipotso tsa patlisiso le foromo ya tumalano ka kitso mo teng ga lebokoso le le notletsweng le le kannweng le le beilweng foo. O ka nna wa boloka phamfolete eno ya tshedimosetso. Tsweetswee romela pampiri ya dipotso tsa patlisiso le foromo ya tumelelo ka kitso pele ga 17:00 ka Labotlhano. O ka nna wa ikgogela morago mo patlisisong eno nako nngwe le nngwe morago ga go simolola pampiri ya dipotso tsa patlisiso go fitlha o e romela. E re ka re ka se ka ra kgona go golaganya tshedimosetso e o re nayang yone le wena, ga o kitla o kgona go tlosa tshedimosetso ya gago mo patlisisong fa o sena go e romela.

**Maikarabelo a babatlisisi ke afe?**

- Maikarabelo a babatlisisi ke go tlhomamisa gore patlisiso e dirwa tumalanong le melao ya patlisiso, gore go se ka ga itsiwe gore eno ke tshedimosetso ya gago le go e boloka e le

khupamarama, mme kwa bofelong go go naya pegelokarabo ka dipholo tsa patlisiso fa o di batla.

**A o tla tswela ke mosola ka go tsaya karolo mo patlisisong?**

- Ga go na mesola ya ka tlhamalalo e o tla e bonang jaaka motsayakarolo. Mme go tsaya karolo ga gago go tla tokafatsa go tlhaloganya ga rona tsela e baithuti ba dirisang methylphenidate ka yone le mabaka a go e dirisa. Ka jalo, baagi ba tla tswelwa molemo ke patlisiso eno ka go tsenngwa tirisong ga ditshitshinyo tsa go rotloetsa tiriso e e sireletsegileng ya methylphenidate.

**A go ka nna le dikotsi dipe tsa go tsaya karolo ga gago mo patlisisong eno?**

- Kotsi mo go wena jaaka motsayakarolo ga e kalo mo patlisisong eno. Go tlatsa pampiri ya dipotso tsa patlisiso go ka nna ga go bakela manthata a maikutlo; le fa go ntse jalo, o ka tlhomamisega gore dikarabo tsa gago di tla bolokwa e le khupamarama e go ka se kang ga rothisiwa mmutla madi ka yone. Ga o kitla o botswa tshedimosetso epe ya poraefete e bile dikarabo tsa gago ga di ka ke tsa latedisiwa go bona gore e ne e le tsa gago. Mo godimo ga moo, fa o ka ikutlwa o sa phuthologa go araba potso epe, o ka nna wa tlhopha go e tlola. Gape o ka nna wa ikgogela morago mo patlisisong gotlhelele.

**Ke mang yo o tla kgonang go bona tshedimosetso?**

- Tshedimosetso yotlhe e tla bolokwa e le khupamarama gotlhelele mme e tla bolokwa mo khomphiutheng e e sireleditsweng ka khunololamoraba mo ofiseng e e notletsweng. Batho ba e leng bone fela ba ba tla dirang ka tshedimosetso e o re nayang yone e tla nna setlhopha sa patlisiso le mogakolodi yo o tlhatlhobang thutatshelo ka go dirisa dipalo. Ga go na motsayakarolo ope yo o ka tlhaolwang ka tshedimosetso e a re neileng yone. Ka ntlha ya moo, motsayakarolo ga a kitla e itsiwe ka leina gotlhelele e bile ga go na motsayakarolo ope yo o ka tlhaolwang mo kgatisong epe fela ya dipholo.

**Ke mang yo o ka tlhatlhobang direkoto tsa patlisiso?**

- Direkoto tsa patlisiso di ka tlhatlhobiwa ke Komiti ya Maitshwaro a a Siameng ya Patlisiso ka tsa Pholo.

**Maloko a setlhopha sa patlisiso ke bomang mme dithutego tsa bone ke dife?**

- Moeteledipele wa porojeke: Ngaka JR Burger (BPharm, MPharm, PhD)
- Mmatlisisi/ Moithuti wa morago ga kalogo: J Dreyer (BPharm)
- Motlhokomedi-mmogo wa badiri: Mohumagadi I Kotze (BPharm, MBA)
- Motlhokomedi-mmogo wa badiri: Mop S van Dyk (BPharm, MSc, PhD)

**Go tla diregang fa o ka ikutlwa o sa phuthologa ka tsela nngwe e le se ka tlhamalalo se bakwang ke go tsaya karolo ga gago mo thuto-patlisisong eno?**

- Fa potso nngwe e e rileng e dira gore o ikutlwe o sa phuthologa, o ka nna wa e tlola mme o fetele kwa potsong e e latelang. Kgotsa, o ka nna wa ikgogela morago mo patlisisong kwantle ga kotlhao. Fa o tshwenyega malebana le tsela e o dirisang methylphenidate ka yone kgotsa o tshwenyegile mo maikutlong, o ka nna wa etela [redacted] kgotsa o ikgolaganye le bone mo nomoreng ya [redacted].

**A o tla duelelwa go tsaya karolo mo patlisisong eno gape a o tla nna le ditshenyegelo dipe?**

- Nnyaa, ga o kitla o duelelwa go tsaya karolo mo patlisisong eno e bile ga o kitla o nna le ditshenyegelo dipe ka ntlha ya go tsaya karolo mo patlisisong eno.

**A go na le se sengwe se o tshwanetseng go se itse kgotsa go se dira?**

- Fa o kopana le mathata ape kgotsa o na le dipotso dipe ka tumelelo ya gago kgotsa patlisiso, o ka ikgolaganya le moeteledipele wa porojeke, Ngaka JR Burger mo atereseng ya Johanita.Burger@nwu.ac.za kgotsa mo nomoreng ya 018 299 2285.
- Gape o ka ikgolaganya le Komiti ya Maitshwaro a a Siameng ya Patlisiso ka tsa Pholo ya Legoro la Disaense tsa Pholo ka go dirisa Mohumagatsana Carolien van Zyl mo nomoreng ya +27 18 299 2094 kgotsa mo atereseng ya Carolien.VanZyl@nwu.ac.za fa o na le matshwenyego ape kgotsa dingongorego tse di iseng di rarabololwe ka mo go lekaneng ke mmatlisisi.
- O tla newa khopi ya tshedimosetso eno le foromo ya tumelelo gore o di boloke mo direkotong tsa gago.
- Go tla neelwa puo kwa dihoseteleng tsotlhe tse di tsayang karolo malebana le tiriso ya methylphenidate, dikotsi tsa teng le ka fa molao o lebang tiriso ya yone ka gone.
- Diphitlhelelo tsa patlisiso di tla bolelelwa Modini wa Moithuti yo o tla bolelelang dikomiti tsa hosetele dipholo.
- Gape o tla bolelelwa diphitlhelelo tsa patlisiso fa o kgatlhegela go di itse. O ka ikgolaganya le Ngaka JR Burger ka kgang eno mo atereseng ya Johanita.Burger@nwu.ac.za kgotsa mo nomoreng ya 018 299 2285.

# FOROMO YA TUMELELO KA KITSO

## Maikano a motsayakarolo

Ka go saena fa tlase, Nna ……..…… ke dumalana go tsaya karolo mo thutopatlisisong ya setlhogo se se reng: Go ipega ga baithuti ba hosetele gore ba dirisa methylphenidate kwa setheong sa akatemi sa thešiari ya Aforikaborwa.

**Ke ikana fano gore:**

- Ke buisitse tshedimosetso eno le foromo ya tumelelo le gore e kwadilwe ka puo e ke kgonang go e bua sentle kwantle ga bothata.
- Ke neilwe tshono ya go botsa dipotso mme dipotso tsotlhe tsa me di arabilwe ka botlalo.
- Ke a tlhaloganya gore go tsaya karolo mo patlisisong eno ke ga boithaopo e bile ga ke a gatelelwa gore ke tseye karolo.
- Nka nna ka tlhopha go tswa mo patlisisong nako nngwe le nngwe pele ke romela pampiri ya dipotso tsa patlisiso le gore ga ke kitla ke otlhaiwa kgotsa ke tshwarwa ka tsela e e sa siamang ka gope.

E saenilwe kwa (lefelo) .....…..…….. ka (*letlha*) ……...……..2015.

..... .....

**Mosaeno wa motsayakarolo** **Mosaeno wa mosupi**

## Maikano a motho yo a amogelong tumelelo ya katiso

Nna, (leina) ....., ke ikana gore:

- Ke tlhaloseditse motsayakarolo tshedimosetso mo tokomaneng eno (leina) .....
- Ke mo rotloeditse go botsa dipotso mme ka tsaya nako e e lekaneng go di araba
- Ke kgotsofaletse gore o tlhaloganya ka botlalo dikarolo tsotlhe tsa patlisiso, jaaka di tlotlilwe fa godimo
- Ga ke a dirisa motoloki ope

E saenilwe kwa (lefelo) .....…..…….. ka (*letlha*)……...……...2015

..... .....

**Mosaeno wa motho yo a amogelong tumelelo ya katiso** **Mosaeno wa mosupi**

## Maikano a mmatlisisi

Nna, J Dreyer, ke ikana gore:

- Ke tlhaloseditse motsayakarolo tshedimosetso mo tokomaneng eno (leina) .....
- Ke mo rotloeditse go botsa dipotso mme ka tsaya nako e e lekaneng go di araba
- Ke kgotsofaletse gore o tlhaloganya ka botlalo dikarolo tsotlhe tsa patlisiso, jaaka di tlotlilwe fa godimo
- Ga ke a dirisa motoloki ope

E saenilwe kwa (lefelo) .....…..…….. ka (*letlha*) ……...……...2015

..... .....

**Mosaeno wa mmatlisisi** **Mosaeno wa mosupi**

# Pampiri ya dipotso tsa patlisiso ka Ritalin®/Concerta®

Re lebogela go amogela ga gago pampiri eno ya dipotso tsa patlisiso!

Pampiri eno ya dipotso tsa patlisiso e na le dikarolo di le nne. Karolo A ke ya tshedimosetso ka motsayakarolo. Karolo B e botsa dipotso tsa gore baithuti ba dirisa jang methylphenidate le gore ke eng fa ba e dirisa. Methylphenidate ke setlhare se se tlhagafatsang motho se motho a se newang ke ngaka se se dirisediwang go alafa Go sa kgone go tlhoma mogopolo/ Bothata jwa Matlhagatlhaga a a Feteletseng kgotsa Bothata jwa go sa kgone go Tlhoma Mogopolo, e leng Attention Deficit/ Hyperactivity Disorder or Attention Deficit Disorder (ADHD kgotsa ADD). Ka dinako tse dingwe, batho gape ba dirisetsa methylphenidate mabaka a mangwe. Mainakgwebo a methylphenidate ke Ritalin®, Ritalin LA®, Methylphenidate HCL Douglas® le Concerta®. Karolo C e amana le kwa baithuti ba bonang methylphenidate gone. Karolo ya bofelo, Karolo D, e amana le ka fa o ikutlwang ka gone ka methylphenidate.

Tsweetswee buisa potso nngwe le nngwe o bo o tlatsa karabo e e boammaaruri go di feta tsotlhe mo go wena. Naya karabo e le nngwe mo potsong nngwe le nngwe ntle le fa go laetswe ka tsela e sele. Supa karabo ya gago ka go thala sefapaano mo lebokosong. Kgopolo ya gago e botlhokwa thata mo go rona mme ka jalo go bothokwa gore o bue boammaaruri ka moo o ka kgonang ka gone.

Patlisiso eno ke ya boithaopo gotlhelele. O ka nna wa tlhopha go ikgogela morago nako nngwe le nngwe pele o romela pampiri ya dipotso tsa patlisiso mme gape o ka tlhopha go tlola potso fa o ikutlwa o sa phuthologa go e araba.

Re lebogela nako ya gago. Go tsaya karolo ga gago go anaanelwa thata!

# Pampiri ya dipotso tsa patlisiso ka Ritalin®/Concerta®

| Nomore ya pampiri ya patlisiso | |
|---|---|

KAROLO A: Dipotso tse di amanang le motsayakarolo

Tsweetswee re bolelele ka ga gago.

(1) O tla bo o le dingwaga tse kae kwa bokhutlong jwa 2015? Dingwaga di le ____

(2) O mo ngwageng ofe wa dithuto? Ngwaga wa bo ____

| (3) | A o monna kgotsa mosadi? |
|---|---|
| 1 | Monna |
| 2 | Mosadi |

| (4) | O mo legorong lefe? |
|---|---|
| 1 | Diatshe |
| 2 | Disaense tsa Ikonomi le Botsamaisi |
| 3 | Disaense tsa Thuto |
| 4 | Boenjenere |
| 5 | Disaense tsa Pholo |
| 6 | Molao |
| 7 | Disaense tsa Tlhago |
| 8 | Thutabomodimo |

KAROLO B: Tiriso ya Methylphenidate

**Gakologelwa**:

Mainakgwebo a **methylphenidate** ke: Ritalin®, Ritalin LA®, Methylphenidate HCL Douglas® le Concerta®.

**Modiredi wa tlhokomelo ya pholo** ke motho yo o nang le thutego ya go lemoga Go sa kgone go tlhoma mogopolo/ Bothata jwa Matlhagatlhaga a a Feteletseng kgotsa Bothata jwa go sa kgone go Tlhoma Mogopolo, e leng Attention Deficit/ Hyperactivity Disorder or Attention Deficit Disorder (ADHD kgotsa ADD). Ka sekai ngaka ya malwetse ka kakaretso, ngaka ya malwetse a tlhaloganyo, ngaka ya malwetse a bana, jj.

**Boikaelelo jwa tsa kalafi bo raya** go dirisetsa setlhare lebaka le motho yo o go nayang sone a reng o se dirisetse lone. Ka sekai go dirisetsa methylphenidate ADHD.

**Boikaelelo jo e seng jwa tsa kalafi bo raya** go dirisetsa setlhare mabaka a mangwe e seng a go newa setlhare seo ga gago, jaaka gore o se ka wa robala mme o fetse nako e le kwa phating.

**Motho yo o ntshang setlhare** ke motho (ka sekai ngaka ya malwetse ka kakaretso, ngaka ya malwetse a tlhaloganyo, ngaka ya malwetse a bana, jj.) yo o go bolelelang gore o dirise setlhare sefe

**Lekwalo la setlhare sa kalafi** ke tokomane e e kwadilweng ke motho yo o go nayang setlhare, e e yang go mokhemisi, ya ditaelo tsa go ntshiwa ga setlhare.

| | |
|---|---|
| (5) | A modiredi wa tlhokomelo ya pholo O KILE a kaya gore Ga o kgone go tlhoma mogopolo/ o na le Bothata jwa Matlhagatlhaga a a Feteletseng kgotsa Bothata jwa go sa kgone go Tlhoma Mogopolo, e leng Attention Deficit/ Hyperactivity Disorder or Attention Deficit Disorder (ADHD kgotsa ADD)? |
| 1 | Ee |
| 2 | Nnyaa |
| 3 | Ga ke itse |

| (6) | A O KILE wa dirisa methylphenidate? |
|---|---|
| 1 | Ee |
| 2 | Nnyaa |

| (7) | O dirisitse methylphenidate leng la ntlha? |
|---|---|
| 1 | Pele ga sekolo sa poraemari |
| 2 | Kwa sekolong sa poraemari |
| 3 | Kwa sekolong se segolo |
| 4 | Kwa yunibesiting |
| 5 | Lefelo le lengwe, *tsweetswee tlhalosa* _____ |
| 6 | *Ga ke ise ke ko ke dirise methylphenidate* |

| (8) | A o dirisitse methylphenidate ka nako ya fa o ne o le kwa yunibesiting? |
|---|---|
| 1 | Ee |
| 2 | Nnyaa |

| (9) | O neilwe **lekwalo la setlhare sa kalafi** gantsi go le go kae la methylphenidate e o e dirisitseng? |
|---|---|
| 1 | Ka dinako tsotlhe |
| 2 | Ka gale |
| 3 | Ka dinako tse dingwe |
| 4 | Ka sewelo |
| 5 | Ga go ise go direge |
| 6 | *Ga ke ise ke ko ke dirise methylphenidate* |

(10) O dirisitse methylphenidate gantsi go le go kae **e o neilweng lekwalo la yone**? Tshwaya lebokoso le le tshwanelang go a feta otlhe la mola mongwe le mongwe. Fa e le gore ga o ise e ke o newe lekwalo la setlhare sa kalafi sa methylphenidate tsweetswee tshwaya kholomo ya bofelo.

| | **Ka dinako tsotlhe** | **Ka gale** | **Ka dinako tse dingwe** | **Ka sewelo** | **Ga go ise go direge** | ***Ga ke ise ke ko ke kwalelwe molemo wa kalafi wa methylphenidate*** |
|---|---|---|---|---|---|---|
| O ne o **kwaletswe** sa **bontsi jo bo kae**? | | | | | | |
| Go se dirisetsa boikaelelo **jo e seng jwa tsa kalafi** (lebaka le lengwe le e seng la motho yo o go neileng setlhare, s.k. gore o se ka wa robala, kgotsa go feta nako e ntsi o le kwa phating, jj.) | | | | | | |

| (11) | Ka gale o dirisa methylphenidate gantsi go le go kae? *Tshwaya mabokoso otlhe a a maleba mo go wena.* |
|---|---|
| 1 | Letsatsi le letsatsi |
| 2 | Ka mafelobeke |
| 3 | Pele ga ditlhatlhobo tsa phaposiborutelong |
| 4 | Pele ga ditlhatlhobo tsa kotara |
| 5 | Pele ga ditlhatlhobo |
| 6 | *Ga ke ise ke ko ke dirise methylphenidate* |

(12) FA o KILE wa dirisa methylphenidate, **goreng o ne o e dirisa**? *Tshwaya mabokoso otlhe a a maleba mo go wena.*

| | **Ka dinako tsotlhe** | **Ka gale** | **Ka dinako tse dingwe** | **Ka sewelo** | **Ga go ise go direge** | ***Ga ke ise ke ko ke dirise methylphenidate*** |
|---|---|---|---|---|---|---|
| Go ithuta | | | | | | |
| Gore ke tlhapelwe ke yone | | | | | | |
| Go tokafatsa kgono ya go tlhoma mogopolo | | | | | | |
| Gore ke nne nako e ntsi kwa phating | | | | | | |
| Go fokotsa boima jwa mmele | | | | | | |
| Go itshidila mmele botoka | | | | | | |
| Ka ntlha ya tlhotlheletso ya dithaka | | | | | | |
| Ka ntlha ya ADHD kgotsa ADD ya me | | | | | | |
| Lebaka le lengwe, *tsweetswee le tlhalose* _____ _____ | | | | | | |

(13) Ke **dikuno** dife tse o di dirisang mme gantsi o dirisa di le kana kang ka letsatsi? Tshwaya mabokoso otlhe a a maleba mo go wena. Bolela gore ke dikuno dife tse o di dirisitseng mme o tlatse palogotlhe ya dipilise tse gantsi o di nwang mo letsatsing le le lengwe.

| Tsh | Kuno | Palo ya dipilisi ka letsatsi |
|---|---|---|
| | Ritalin 10mg® | Dipilisi di le ___ ka letsatsi |
| | Ritalin LA 20mg® | Dipilisi di le ___ ka letsatsi |
| | Ritalin LA 30mg® | Dipilisi di le ___ ka letsatsi |
| | Ritalin LA 40mg® | Dipilisi di le ___ ka letsatsi |
| | Methylphenidate HCL Douglas 10mg® | Dipilisi di le ___ ka letsatsi |
| | Concerta 18mg® | Dipilisi di le ___ ka letsatsi |
| | Concerta 27mg® | Dipilisi di le ___ ka letsatsi |
| | Concerta 36mg® | Dipilisi di le ___ ka letsatsi |
| | Concerta 54mg® | Dipilisi di le ___ ka letsatsi |
| | Ga ke itse gore ke dirisa kuno efe | |
| | *Ga ke ise ke ko ke dirise methylphenidate* | |

(14) O nwa jang (di)kuno e o e dirisang/dirisitseng? *Tshwaya mabokoso otlhe a a maleba mo go wena.*

| Kuno | Kometsa | Sunetsa | Tlhaba lemao | Tsela e nngwe *(tsweetswee tlhalosa gore jang)* |
|---|---|---|---|---|
| Ritalin 10mg® | | | | |
| Ritalin LA 20mg® | | | | |
| Ritalin LA 30mg® | | | | |
| Ritalin LA 40mg® | | | | |
| Methylphenidate HCL Douglas 10mg® | | | | |
| Concerta 18mg® | | | | |
| Concerta 27mg® | | | | |
| Concerta 36mg® | | | | |
| Concerta 54mg® | | | | |
| Ga ke itse gore ke dirisa kuno efe | | | | |
| *Ga ke ise ke ko ke dirise methylphenidate* | | | | |

KAROLO C: Go bona methylphenidate

(15) Gantsi o bone methylphenidate ya gago go tswa kae? *Tshwaya mabokoso otlhe a a maleba mo go wena.*

| | **Ka dinako tsotlhe** | **Ka gale** | **Ka dinako tse dingwe** | **Ka sewelo** | **Ga go ise go direge** | ***Ga ke ise ke ko ke dirise methylphenidate*** |
|---|---|---|---|---|---|---|
| Kwa khemising ka lekwalo la setlhare sa kalafi le le kwadilweng ke motho yo o ntshang setlhare | | | | | | |
| Kwa khemising ka lekwalo la setlhare sa kalafi le e seng la nnete | | | | | | |
| Kwa khemising kwantle ga lekwalo la setlhare sa kalafi | | | | | | |
| Ditsala | | | | | | |
| Lelapa | | | | | | |
| Inthanete | | | | | | |
| Lefelo le lengwe, *tsweetswee le tlhalose* _____ | | | | | | |

(16) **Fa o ne o batla**, a o akanya gore o ne o ka bona methylphenidate go tswa? Tlhopha 'Ee' mo go tsotlhe tse di leng boammaaruri mo go wena le 'Nnyaa' mo go tsotlhe tse di seng boammaaruri mo go wena.

| **Ee** | **Nnyaa** | |
|---|---|---|
| | | Khemisi **ka lekwalo la setlhare sa kalafi** le le kwadilweng ke **motho yo o ntshang setlhare** |
| | | Kwa khemising **ka lekwalo la setlhare sa kalafi le e seng la nnete** |
| | | Kwa khemising **kwantle ga lekwalo la setlhare sa kalafi** |
| | | Ditsala |
| | | Lelapa |
| | | Inthanete |
| | | Lefelo le lengwe, *tsweetswee le tlhalose* _____ |

Mo dipotsong di le mmalwa tse di latelang, tsweetswee kwala boleng jwa gore o dumalana kgotsa ga o dumalane go le go kae le dipoleo tse di latelang.

| | | **Ga ke dumalane gotlhelele** | **Ga ke dumalane** | **Ga ke itse** | **Ke a dumalana** | **Ke dumalana aka botlalo** |
|---|---|---|---|---|---|---|
| (17) | Go motlhofo thata go bona methylphenidate | | | | | |
| (18) | Go motlhofo go bona motho yo o ntshang setlhare (s.k. ngaka) gore a go kwalele lekwalo la go newa methylphenidate, tota le fa moithuti a sena ADD/ADHD. | | | | | |

KAROLO D: Kgopolo ya gago ka methylphenidate

(19) Go ya ka fa o itseng ka gone, o nnile le maitemogelo a dilo tse di latelang gantsi go le go kae ka ntlha ya go dirisa methylphenidate? *Tshwaya mabokoso otlhe a a maleba mo go wena*.

| | **Ka dinako tsotlhe** | **Ka gale** | **Ka dinako tse dingwe** | **Ka sewelo** | **Ga go ise go direge** | ***Ga ke ise ke ko ke dirise methylphenidate*** |
|---|---|---|---|---|---|---|
| *Go opiwa ke tlhogo* | | | | | | |
| *Ditlhabi mo maleng* | | | | | | |
| *Go tlhotlhonelwa* | | | | | | |
| Go fokotsega ga keletso ya dijo | | | | | | |
| Go sa kgone go robala | | | | | | |
| Sedidi | | | | | | |
| Go uba ka bonako ga pelo | | | | | | |
| Go sa ritibale | | | | | | |
| Kgalefo | | | | | | |
| Tse dingwe, *tsweetswee di tlhalose*_____ | | | | | | |

*Mo dipotsong di le mmalwa tse di latelang, tsweetswee bolela gore a o akanya gore polelo nngwe le nngwe e boammaaruri kgotsa maaka.*

| | | **Boammaaruri** | **Maaka** | **Ga ke itse** |
|---|---|---|---|---|
| (20) | Go dirisa methylphenidate kwantle ga lekwalo la setlhare sa kalafi ga go ka fa molaong | | | |
| (21) | Methylphenidate e ka dirisediwa go godisa mesifa | | | |
| (22) | Methylphenidate e ka go tshwarisa tlala | | | |
| (23) | Methylphenidate e ka go otsedisa | | | |

Jaanong patlisiso e fedile! Gakologelwa gore ga o kitla o kgona go tlosa tshedimosetso ya gago fa o sena go romela pampiri ya gago ya dipotso tsa patlisiso kwa meiteroneng wa hostele, ka gonne re ka se kgone go latedisa tshedimosetso gore a ke ya gago.

Re lebogela nako ya gago le go tsaya karolo ga gago!

# ANNEXURE G: CERTIFICATE OF ETHICAL APPROVAL

NORTH-WEST UNIVERSITY
YUNIBESITI YA BOKONE-BOPHIRIMA
NOORDWES-UNIVERSITEIT

Private Bag X6001, Potchefstroom
South Africa 2520

Tel: (018) 299-4900
Faks: (018) 299-4910
Web: http://www.nwu.ac.za

**Ethics Committee**
Tel +27 18 299 4849
Email Ethics@nwu.ac.za

ETHICS APPROVAL OF PROJECT

The North-West University Research Ethics Regulatory Committee (NWU-RERC) hereby approves your project as indicated below. This implies that the NWU-RERC grants its permission that provided the special conditions specified below are met and pending any other authorisation that may be necessary, the project may be initiated, using the ethics number below.

**Project title:** Self-reported use of methylphenidate by hostel students at a South African tertiary academic institution

**Project Leader:** Dr JR Burger

Ethics number: N W U - 0 0 1 4 6 - 1 4 - A 1
(Institution | Project Number | Year | Status)
Status: S = Submission; R = Re-Submission; P = Provisional Authorisation; A = Authorisation

**Approval date:** 2014-11-12 **Expiry date:** 2017-11-30

Special conditions of the approval (if any): None

General conditions:

*While this ethics approval is subject to all declarations, undertakings and agreements incorporated and signed in the application form, please note the following:*

- *The project leader (principle investigator) must report in the prescribed format to the NWU-RERC:*
  - *annually (or as otherwise requested) on the progress of the project,*
  - *without any delay in case of any adverse event (or any matter that interrupts sound ethical principles) during the course of the project.*
- *The approval applies strictly to the protocol as stipulated in the application form. Would any changes to the protocol be deemed necessary during the course of the project, the project leader must apply for approval of these changes at the NWU-RERC. Would there be deviated from the project protocol without the necessary approval of such changes, the ethics approval is immediately and automatically forfeited.*
- *The date of approval indicates the first date that the project may be started. Would the project have to continue after the expiry date, a new application must be made to the NWU-RERC and new approval received before or on the expiry date.*
- *In the interest of ethical responsibility the NWU-RERC retains the right to:*
  - *request access to any information or data at any time during the course or after completion of the project;*
  - *withdraw or postpone approval if:*
    - *any unethical principles or practices of the project are revealed or suspected,*
    - *it becomes apparent that any relevant information was withheld from the NWU-RERC or that information has been false or misrepresented,*
    - *the required annual report and reporting of adverse events was not done timely and accurately,*
    - *new institutional rules, national legislation or international conventions deem it necessary.*

The Ethics Committee would like to remain at your service as scientist and researcher, and wishes you well with your project. Please do not hesitate to contact the Ethics Committee for any further enquiries or requests for assistance.

Yours sincerely

Linda du Plessis

Digitally signed by Linda du Plessis
DN: cn=Linda du Plessis, o=NWU, ou=Vaal Triangle Campus, ou=Vice-Rector: Academic, email=linda.duplessis@nwu.ac.za, c=ZA
Date: 2014.12.02 18:50:50 +02'00'

**Prof Linda du Plessis**
*(chair NWU Research Ethics Regulatory Committee (RERC)*

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