

**Proportional determination and reasons for medication returns at a
tertiary academic hospital in Gauteng**

by

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Plagiarism declaration

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Abstract

South Africa has a quadruple burden of disease which leads to increased pharmaceutical expenditure on communicable and non-communicable diseases. This study aimed to determine the proportion of patients that return unused or expired medicine to a tertiary academic hospital pharmacy in Gauteng, including the reasons for unused or expired medicine being returned. In addition the monetary value of the returned medication was calculated. Furthermore, common medicine disposal practices were assessed. Data was collected by administering questionnaires to patients presenting at the Steve Biko Academic Hospital pharmacy awaiting prescription refills, or those attending for the purpose of returning unused medications.

It was found that the proportion of patients returning unused or expired medicine was approximately 20% ($P \sim 0.2$). Cited reasons for accumulating expired medicine included non-adherence (36%), doctor discontinued treatment (16%), undesirable side effects (12%), death (8%), oversupply (12%), incorrect medicine supplied (4%), short expiry of compounded medicine (4%), unknown reasons (4%), duplication from public and private sector (4%). The monetary value of all returned medicine during the two-week collection period (6 – 17 March 2017) was determined to be R652.11. This value may seem low, but did not include expired or returned medicine from hospital wards, where the usage are different compared to an out-patient setting.

Cardiovascular (11.8%), anti-diabetic (11.8%), corticosteroid (11.8%) and respiratory agents (11.8%) were among the leading medicine class returned. During the previous year (2016), more than three quarters (34.7%) of the patients were in possession of unused and expired medicine, of which only 13.6% returned medicine to pharmacy for safe disposal. Other disposal practices consisted of flushing down the toilet/ in drain (43.2%), discarding in refuse bins (34.1%), throwing it into pit-toilets or burying underground (6.8%), and storing for future use (2.3%).

It was evident from this study that only a small proportion of patients returned unused or expired medicine to pharmacy for safe disposal. The principle reasons for medicine accumulation indicate non-adherence and treatment discontinuation. This study elucidated to the fact that there is a need to educate the public on the importance of proper storage, safe disposal practices, adherence to prescribed

treatment, and to increase locations where unused or expired medicines may be dropped off for safe disposal.

Keywords: Disposal practices, expired medicine, medicine wastage, non-adherence, pharmaceutical waste, returned medicine, unused medicine,

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List of abbreviations

AIDS	Acquired immunodeficiency syndrome
API	Active pharmaceutical ingredient
ART	Antiretroviral therapy
ARV	Antiretroviral
CCMDD	Centralized chronic medicine dispensing and distribution program
CEO	Chief executive officer
DHB	District health board
EML	Essential medicine list
€	Euro
GPP	Good pharmacy practice
HIV	Human immunodeficiency virus
ID	Identity document
IV	Intravenous
MYR	Malaysia ringgit
NHI	National health insurance
NHS	National health system
NZD	New Zealand dollar
PBS	Pharmaceutical benefit scheme
PNHS	Portugal national health service
£	Pound
RPDU	Robotic prescription dispensing units
SAMF	South African medicine formulary
SAS	Statistical analysis software
SBAH	Steve Biko academic hospital
TB	Tuberculosis
UK	United Kingdom
UNICEF	United nations children's fund
USA	United States of America
\$	United State dollar
WHO	World Health Organisation

Glossary

Adherence: The extent to which patients are able to follow the recommendations for prescribed treatment.

Compliance: Similar to adherence and describes the degree to which a patient correctly follows medical advice

Essential medicine list: Medicines that are intended to be available within the context of a functioning health systems at all times in adequate quantities, appropriate dosage form, with assured quality and at a price the community can afford.

Medicine supply chain: The process of forecasting, procurement, storage, and distribution to the patient for final use.

Medicine wastage: Medications which expire or remain unused throughout the whole medicine supply chain.

Non adherence: The extent to which the patient fail to follow recommendations for prescribed treatment under limited supervision

Polypharmacy: The practice of administering many different medicines, especially concurrently, for the treatment of a single disease.

Rational use of medicine: The rational use of medicine requires a patient to receive treatment which is appropriate for the intended condition, adjusted to their individual requirements, for an adequate period of time, and at an affordable cost.

Chapter 1: Background and literature review

Medicine wastage according to West *et al.* is defined as medications which expire or remain unused throughout the whole medicine supply chain.⁽¹⁾ Medicine supply chain entails forecasting, procurement, storage, and distribution to the patients. Medicine wastage also refers to the unnecessary consumption of medicine by patients, or the unjustified non-adherence to treatment guidelines by healthcare professionals.⁽¹⁾ The impact of medicine wastage on the healthcare budget has been described in several countries worldwide.⁽²⁻⁴⁾ In the past decade, South Africa has experienced a significant increase in patients requiring chronic treatment due to life style diseases and the introduction of universal access to antiretroviral therapy (ART). The increasing cost of providing healthcare services to its citizens is the result of growing demand of medicine supply and population explosion. The Health budget in Gauteng has increased from R37 billion in 2016/17 to R46.4 billion in 2018/19.⁽⁵⁾ The influx of patients from other countries and rural areas of South Africa to the metropolitan areas has led to a constant upsurge in the budget allocation for pharmaceuticals on an annual basis.

Gauteng is the most highly populated province. This has an impact on the provincial expenditure in terms of the health budget allocation, national fiscal, health service delivery and medicine cost to government. In 2015/16, the Gauteng health budget was approximately R34.2 billion.⁽⁶⁾ Other factors responsible for the escalating medicine cost include overpriced marketing practices, the lack of generic alternatives for newly registered products resulting from long term patent rights, supply chain irregularities and mismanagement of resources, the high cost of research and drug development, as well as medicine wastage by patients.⁽³⁾ Unused and expired medicine may impose a significant additional financial burden on the government's proposed National Health Insurance (NHI) scheme.⁽⁷⁾ The NHI is a health system financing model that will ensure that all South African citizens and long term or permanent residents are provided with quality, essential healthcare, regardless of their employment status and ability to make a direct monetary contribution to the NHI Fund as envisaged in the bill of rights.⁽⁷⁾

There are several reasons for accumulation of unused and expired medicine in patients home. Several studies around the world identified reasons for medicine return and disposal practices.^(3, 8-18) The proportion of medicine return and reasons for medicine return at Steve Biko Academic Hospital (SBAH) is unknown.

1.1. The South African health setting

South Africa's health system consists of different levels of healthcare facilities. These are divided into private health facilities (pharmacies, private doctors and private hospitals) and public health facilities (government hospitals, pharmacies and clinics). The public health system is classified according to the level of care which each facility provides. Primary healthcare clinics form the foundation of the entire system. Services rendered includes, but is not limited to, antenatal care, family planning, child healthcare (immunization and growth monitoring), basic healthcare (management of non-complicated non-communicable diseases), and addressing the burden of disease (screening, prevention and treatment of tuberculosis (TB), human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS). The South African government has a constitutional responsibility as stated in section 27 of the constitution, to provide quality and accessible public healthcare services to its citizens without cost.⁽¹⁹⁾

The majority of primary healthcare clinics and health centers are mostly managed by registered nurses with or without a post basic pharmacist assistant, community service pharmacist or a visiting doctor. The majority of the health care clinics are found in rural areas. When patients require more specialized treatment, primary care clinics will refer them to a secondary (district and regional) hospital. Provincial and tertiary hospitals provide advanced surgical, diagnostic procedures and treatment that are not available at the primary or secondary level. It is estimated that the South African government currently financially subsidizes approximately 81% of the population whilst only 17% depend on private healthcare, where users pay for services rendered. ^(20, 21) In Gauteng, national statistics indicate a slightly different pattern where 74% are dependent on public healthcare and almost 25% make use of private healthcare. Public health services are responsible for almost 11% of the

government's total budget.⁽²²⁾ As a result of the current unfavorable socio-economic climate in South Africa, the 2016 budget speech has shown that government is exploring avenues to reduce cost and curtail spending in different sectors in order to improve the efficiency and quality of health service delivery. ⁽²²⁾

One initiative is the implementation of the centralized chronic medicine dispensing and distribution program (CCMDD). CCMDD is a program whereby chronic medication is delivered to community based pick up points by a contracted service provider and patients obtain the medication from this point rather than at a health facility.⁽²³⁾ This program will see more than 2 million patients collecting their chronic and antiretroviral medication at a central location/pick up point such as schools, churches and community pharmacies. This program will be controlled through private-public partnership (PPP) and is envisaged to reduce the patient burden at district, regional and tertiary hospitals. Such a partnership will increase number of patients with chronic diseases to access medication, provide the uninterrupted availability and adequate supply of ARVs and limit organizational issues such as the lack of human resources frequently experienced in the public health system.^(23, 24) Another aspect regarding prescribing practices contained in the Medicine and Related Substance Control Act 101 of 1965 (as amended), makes provision for certain schedules of chronic medicine to be repeated five times (6 months prescription). However, the medicine supplied may not exceed quantities sufficient for 30 days of uninterrupted treatment. This results in patients having to attend the hospital or clinics every month only for the collection of medicine.⁽²⁵⁾

1.2. Medicine wastage

Medicine wastage is a global problem and has a significant impact on the annual health budget estimation and allocation. It is one of the principal contributors to the escalation of pharmaceutical costs, locally and internationally.^(1, 3, 26) Medicine wastage imposes a financial burden on both patients and the government.⁽¹⁾ Medicine shortage in South Africa is a common phenomenon and has a direct impact on health-seeking behavior since patients suffering from chronic conditions require uninterrupted treatment.⁽²⁷⁾ Medicine misuse, underuse and overuse all result in wastage of precious resources and can lead to a wide spread of health and

environmental hazards. Irrational drug use includes the inappropriate use of antibiotics, polypharmacy, inadequate dose, inappropriate self-medication or non-adherence to the treatment regimen.⁽²⁸⁾

1.3. Cost of wasted medicine

1.3.1. Europe

Pooled data from 51 European countries representing a population of 900 million, showed that around 221 million individuals suffering from chronic heart failure required approximately €6.1 billion (R 90.1 billion) worth of medicine.⁽²⁹⁾ Follow up on these expenses calculated the amount of unused drugs to be in the order of €915 million (R13 billion), which roughly represents 2% of the health budget being wasted.⁽²⁹⁾ A study conducted in Portugal, reported that the cost of wasted medicine associated with different pack sizes being dispensed to the same patient was estimated at an average of €1.75 (R26.00), of which 58.5% of these medicines were paid for by the Portugal National Health Service (PNHS).⁽⁴⁾

1.3.2. Saudi Arabia and other Gulf countries

Wastage on the basis of medicine cost is reported to be nearly 25% (\$9.3 million) R134 million in the Persian Gulf countries (Kuwait, Bahrain, Iraq, Oman, Qatar and the United Arab Emirates) compared to 19.2% (\$7.7 million) R111 million in Saudi Arabia.⁽³⁾ The cost of expired, unused medicine was significantly lower in Saudi Arabia than the amount identified in other Gulf countries.⁽³⁾ Combined these seven Arab states spent approximately \$150 million (R17 billion) per year on medicine which was never used and subsequently disposed of.^(3, 9)

1.3.3. New Zealand

Studies conducted in New Zealand estimated medicine wastage cost at about NZD 9 to 11 billion (R78 to R95 billion) per year.⁽¹⁰⁾ Studies conducted in Hutt valley district health board (DHB) region with approximately 51500 households, found the cost of returned medicine to be NZD 17100 over a four week period. ⁽¹⁰⁾

1.3.4. United States of America

It is estimated that almost two thirds (60%) of all prescription medicine issued in the United States of America (USA) is unused and/or wasted. This amounts to nearly 1300 tons of pharmaceuticals annually, with a projected cost of \$2.4-5.4 billion (R28 to 64 billion). The total pharmaceutical expenditure in the USA has increased by 6% from 2009 and 2010, with hospital pharmaceutical expenditure contributing to 1.5% of this increase. The total healthcare spending increased from \$299.2 to \$307.5 billion (R1 to 3 trillion) in the same period. However, the ongoing introduction of generic medicine for commonly used expensive originator products has been seen to slightly moderate the increase in cost. Generic medicine accounted for 78% of all prescription drugs dispensed by the end of 2010 which significantly reduced cost of providing healthcare to the citizens in USA.⁽³⁰⁾

1.3.5. United Kingdom

The National Health Service (NHS) in the United Kingdom (UK) has seen a 55% increase in the number of prescriptions from 1998 until 2009.⁽³¹⁾ It is estimated that it has costed the NHS an additional £150 million (R2 billion) per year in dispensing fees.⁽³¹⁾ This increase is mostly attributed to drugs used in the management of chronic diseases. The UK spends around £8 billion (R142 billion) per annum on pharmaceuticals, of which nearly 585 tons of unused medicines are returned to the point of dispensing for safe disposal.⁽³²⁾ In 2009/10 it was estimated that £300 million (R5 billion) worth of prescribed medicine was discarded in UK.⁽³³⁾ This may be the result of the NHS supplying medicine at no cost to the end-user. Patients that do not pay for their medicine are seen to be contributors of medicine wastage.⁽³³⁾

1.3.6. Malaysia

Pharmaceuticals worth a total of MYR 4362.28 (R13347.60) was wasted in Tuanku Jaafar Seremban Malaysia during the period between June and November 2007, with an average of MYR 42.35 (R129.58) per patient.⁽³⁴⁾ Pharmaceutical expenditure cost the Malaysian government in excess of MYR 59566.50 (R182260.12) annually, with an average of MYR 9927 (R30374.39) per month.⁽³⁴⁾ Population focused on in

the study were hypertension patients visited at home and volunteers who returned medicine to pharmacy for safe disposal at hospital Tuanku Jaafar Seremban.⁽³⁴⁾

1.4. Type of medicine returned

In a study conducted in Kuwait, 95% of respondents reported to have unused or expired medicine which needed to be disposed of. The majority of the medicine (66%) were oral dosage formulations. Among oral dosage formulations; syrups (51%) accounted for the larger proportion of unwanted medicine followed by topical creams or ointment (35%) and drops (32%).⁽¹¹⁾ Metformin, potassium chloride, furosemide, captopril, lovastatin and isosorbide dinitrate were among the top six medicine being returned to the pharmacy for disposal in Malaysia.⁽³⁴⁾ Medicine used in the treatment of chronic diseases (hypertension, diabetes, cholesterol and heart disease) in USA accounted for 17%, with antibiotics, psychotropic and pain medication accounting for the remainder.⁽³⁵⁾

A study conducted in New Zealand found that most returned medicine included paracetamol, diclofenac, simvastatin, calcium carbonate, omeprazole, aspirin and cilazapril.⁽¹⁰⁾ Anti-inflammatory and anti-rheumatic medicine accounted for more than 25% of the wasted medicine in Portugal.⁽⁴⁾ The top drugs being wasted in Saudi Arabia included cardiovascular agents, central nervous system agents, drugs to treat respiratory conditions and antimicrobials.⁽³⁾ According to a recent US Medicare survey in 2016, the most frequent unused medicine or medicine groups leading to accumulation and wastage included analgesics, antibiotics and respiratory tract agents.⁽³⁶⁾ Drugs not used due to changes in medication type and dosage included anti-hypertensives, anti-psychotics, anti-diabetic agents and pain medication.⁽³⁶⁾ In Serbia antibacterial agents were some of the most commonly discontinued medicines.⁽³⁷⁾ It is estimated that in some countries up to 85% of prescribed antibiotics are not used and are either improperly discarded or inappropriately stored.⁽³⁷⁾

1.5. Limiting medicine wastage

It was reported in 2008 that, the UK's national prescribing center published recommendations advocating the acceptability for disease controlled patients with chronic conditions to receive long term treatment (6 months) without the need to collect monthly refills.⁽³²⁾ This controversial proposal was the result of UK patients being despondent with the current 28 day supply of medicine because of costly transportation, limitation in the freedom to travel for prolonged periods and the anxiety caused when medicine ran low over weekends or holidays.⁽³²⁾ Supplying chronic medicine for prolonged periods makes it difficult to measure adherence and was cited to be a major contributor towards medicine accumulation.⁽³²⁾

Recently the South African government implemented automated dispensing units in collaboration with the private sector in selected pilot sites. The initiative was introduced as a possible solution to reduce and prevent medicine wastage.⁽³⁸⁾ These automated units are activated by unique patient identifiers to ensure that registered users can only collect the specified quantity of prescribed chronic medicine from one distribution point once a month.⁽³⁸⁾ Robotic Prescription Dispensing Units (RPDU) has been shown to reduce waiting time, limit medicine duplication, dispensing errors and to reduce medicine accumulation and wastage.⁽³⁸⁻⁴⁰⁾ Another possible solution to limit medicine oversupply, duplication and wastage in areas where automated dispensing is not possible, would be the introduction of an online biometric system or health ID card.

The National Department of Health is currently in the process of conducting pilot studies on the viability of RPDU's, but it is anticipated to remain a logistical challenge until all the provinces are electronically linked with all public patient health records.⁽³⁹⁾ Every public health facility will require a functioning high-speed broadband internet connection to be able to link and exchange data on a national database. Unit dose repackaging may enhance treatment adherence as observed in clinical trials, although patients may find this approach to be laborious.⁽⁴¹⁾ In a study conducted in Kuwait, it was noted that three quarters of the respondents believed that medicine

wastage could be limited or reduced by prescribing and dispensing the exact amount of medicine required to manage a patient for a specified time.⁽¹¹⁾ This response suggests that health facilities tend to oversupply their patients with medication, which contributes to wastage.⁽¹¹⁾

International studies on similar topics have concluded that collaboration between governments and private institutions need to simultaneously address the issue regarding medicine wastage.⁽⁴²⁾

1.6. Reasons for possessing unused or expired medicine

Several reasons for medicine accumulation have been reported in the international literature. Reasons for accumulation and wastage of medicine include the death of a family member, expired medication, change of dosage or therapeutic modification by the prescribing doctor,⁽¹⁰⁾ improved health condition or self-discontinuation, patients forgetting to take prescribed medication,^(43, 44) undesirable side effects,⁽⁴⁴⁾ excess medicine being prescribed or dispensed,^(11-13, 45-47) non adherence and discontinuing medicine treatment after discharge from hospital, felt like my condition was not improving,⁽⁴⁴⁾ reuse or hand over to someone at home with similar symptoms,^(14, 48) or drug pilferage.⁽⁴⁹⁾ In addition, healthcare professionals are partly to blame for irrational and over prescribing practices.⁽⁵⁰⁾ Pharmacists are often reluctant to break the original packaging, or in the case of prescribed solutions and liquids, to decant the specified amount into appropriate containers in order to ensure that the correct amount of medicine is dispensed. This is a common occurrence worldwide.⁽⁵¹⁾ It has been noted in practice that unnecessary treatment is often given only to keep demanding patients satisfied and ensure their return.⁽⁹⁾ Media adverts and celebrity endorsements target patients to seek specific medication from medical practitioners without proper clinical examination. Another principle reason most patients fill their prescriptions irrespective of whether they still have an adequate supply for the month, is the perceived fear that medicine will not be available when they run out of stock.⁽³⁸⁾

In a few instances, the precise reason for wastage and accumulation remains unknown. Patients fail to remember the reason as the time gap between acquisition and return is often too long. This is particularly evident where family members return unused medicine from a deceased relative. Patients also tend to return all their accumulated medicine in one batch, being unable to comment on the individual products and giving one reason irrespective of the number of items in the pack.⁽¹²⁾

The central theme of these studies emphasize a global commonality. It has been noted that where a country provides free healthcare services, such as South Africa, patients often abuse this system in multitudinous manners, often resulting in medicine wastage.⁽³³⁾ Some of the most apparent fashions include multiple visits to one hospital, and frequently switching from one health facility to another.⁽³⁵⁾ The lack of communication between different health establishments has the consequence of patients periodically receiving duplication of the same medication. It is perceived that duplication may occur where individuals believe community and primary healthcare clinics render inferior treatment compared to tertiary institutions or private facilities. The ramification of this double-treatment phenomenon is either unintended accumulation, or deliberate stockpiling of medicine intended for resale or distribution to friends and family members.⁽³⁶⁾

1.6.1. Saudi Arabia

In Saudi Arabia almost half (41.6%) of the patients obtain their medicine from the government, compared to 35.5% receiving it from private facilities.⁽³⁾ Interestingly, 19.4% of the Saudi population receive treatment from both private and public institutions, resulting in medicine duplication and wastage.⁽³⁾ In Saudi Arabia (24.9%) and other Gulf countries (27.6%) it was found that most families did not adhere to their chronic prescription regimens.⁽³⁾ Only 54.8% of people receiving medicine for acute conditions in Saudi Arabia and 43.7% from other Gulf countries indicated that they had completed the full course of treatment as prescribed.⁽³⁾ A similar study conducted in Lithuania showed that 36% of patients did not adhere to their treatment, with no significant difference between males and females.⁽⁴³⁾

1.6.2. Tanzania

Oversupply of medicine (especially antibiotics and cardiovascular agents) was found to be one of the leading reasons contributing to medicine wastage in Tanzania.⁽⁴⁸⁾ Inadequate human resources are often at the center of impairing quality pharmaceutical services being rendered in over-burdened healthcare facilities. The lack of keeping appropriate track of patients and the absence of adequate patient records detailing prescription refill history additionally contribute to medicine accumulation and wastage.⁽⁴⁸⁾

1.6.3. Worldwide

The WHO estimated that more than 50% of all medicine are prescribed and dispensed in an irrational manner, and that half of these patients fail to adhere to their treatment.⁽²⁸⁾

1.6.4. Australia

It was reported in 2015 that treatment hoarding and non-adherence contributed to medicine wastage in Australia.⁽⁴⁹⁾

1.6.5. Netherland

Non-adherence to the prescribed treatment protocols are frequently implicated in the accumulation and wastage of medicine.⁽⁵⁰⁾

1.6.6. United Kingdom

An example of treatment duplication was recently illustrated in a study conducted by the European Society of Cardiology.⁽⁵²⁾ Non-adherence to treatment regimen in Serbia may be exacerbated by different factors such as psychosocial stressors, comorbidity polypharmacy, the type and classification of medicine, patient age, socioeconomic status, and the inappropriate labelling of medicine.⁽³⁷⁾ A report from a study conducted in the UK identified patient initiated treatment discontinuation (self-

cessation) as a result of treatment failure and adverse drug reactions to be a significant contributing factor in medicine accumulation.⁽⁵²⁾

1.6.7. India

An Indian study reported that 10.5% of patients deliberately stockpiled unused or expired medicine for the purpose of reselling back to the pharmacy, which is allowed by law.⁽³²⁾ This practice is however illegal in most other countries, including South Africa.⁽²⁵⁾

1.6.8. Nigeria

In some developing countries in Africa such as Nigeria, it has been reported that medicine wastage are often as the result of bad pharmacy practice and dispensing inconsistencies where medicine are frequently dispensed without indicating the proprietary name or expiry date.⁽¹⁴⁾

1.6.9. United States of America

A study conducted in Pennsylvania found that the reasons cited varied from patients reported not needing all the prescribed agents (26%), dosage changed by the physician (21%), side effects or adverse reaction (22%), and expired medication (3%).⁽³⁶⁾

1.6.10. Lithuania

Reasons for non-adherence consisted of complexity of the daily regimen, distrust in the choice of treatment and expensive medicine.⁽⁴³⁾ It was noted that females were more inclined to check expiry dates on medicine containers compared to their male counterparts.⁽⁴³⁾ It could be argued that women consider themselves as responsible for the medicine cabinet at home.⁽⁴³⁾

1.6.11. Jordan

It was reported in Jordan that hospital patients collected medicine from a window without interacting with the pharmacist. This practice limit the amount of time pharmacists spend with patients posing serious risk of non-adherence due to lack of counselling. ⁽⁴⁸⁾

1.6.12. Serbia

Non-adherence to treatment regimen in may be exacerbated by different factors such as psychosocial stressors, co-morbidity polypharmacy, the type and classification of medicine, patient age, socioeconomic status, and the inappropriate labelling of medicine.

1.7. Legislative requirements on labeling

According to South African good pharmacy practice, labelling of dispensed medicine must be clear, legible in English and any other official language. Letters must be mechanically printed and as far as possible.⁽⁵³⁾ The following information must appear on the label of medicine intended for human use: approved name, patients name, name and business address of the pharmacy, name of the pharmacist, date of dispensing , reference number or script number and direction on how to use such medicine including any warnings such as “this medicine may cause drowsiness”.⁽⁵³⁾ From literature outlined above it is evident that there is a great need for education and counseling regarding adherence to prescribed treatment and the appropriate use of medicine in order to reduce wasteful expenditure.^(14, 29)

1.8. Returning of unused medicine and medicine return programs

Several drug take back or medicine return programs have been implemented in different countries, each with varying success and criteria. In the USA it has been reported that 61% of household members from Oklahoma were compliant in participating in such a program launched by the National Drug Enforcement Administration.⁽⁴⁶⁾ These types of take-back or medicine return programs are

however only effective if all relevant stakeholders, including patients, hospitals, pharmacies, pharmaceutical wholesalers and pharmaceutical waste disposal companies, communicate and work together.⁽⁵⁴⁾

Another drug take-back or medicine return study conducted in the Arabic Sultanate of Oman identified criteria for recyclable and non-recyclable medications.⁽⁹⁾ Recyclable drugs are chemically analyzed for safety, efficacy and stability where after a decision is made to either reject and destroy, or accept and re-introduce the medicine for use.⁽⁹⁾ The rationale for this initiative is to limit unnecessary financial loss, and to reduce the amount of pharmaceuticals contaminating the environment.⁽⁹⁾

In Australia a national return and destruction of unwanted medicine program was initiated in an attempt to prevent improper disposal practices of medicine by discarding in municipal bins and flushing down toilets.⁽²⁶⁾ During the campaign an estimated 600 tons of medicine, amounting to \$2 million (R23.7 million), was reportedly wasted.⁽²⁶⁾ From the collected medicine, salbutamol, insulin, and furosemide were among the top three discarded agents; however these agents may not be representative of the true identifiers, since the amount and type of medicine improperly discarded remains unknown.⁽²⁶⁾ Seventy percent of the improperly discarded medicine was subsidized by the Australian Pharmaceutical Benefit scheme (PBS).⁽²⁶⁾ It was found that out of all returns, 44% of these drugs had not yet reached its expiry date. Most of the discarded medicine were scheduled prescription medicine.⁽²⁶⁾

The destruction of medicine is often a costly procedure and seen as a barrier in the drug take-back or medicine return initiatives. In the Republic of Serbia, pharmacies are lawfully obliged to accept all returned unused or expired medicine from the public.⁽⁵⁵⁾ Upon receipt, it is sent back to the wholesalers or manufacturers, or labeled as pharmaceutical waste destined for destruction.⁽⁵⁵⁾

Patients not being familiar with the correct manner for proper disposal of medication may result in accumulation, medication hoarding and sharing or inappropriately supplying expired medication.⁽⁴⁹⁾ The cost for disposing of the pharmaceutical waste in Croatia and Bosnia and Herzegovina range from US\$2.2/kg to US\$4.1/kg (R26.08/kg to R48.61/kg). In Croatia to incinerate the current stockpile of waste pharmaceuticals they accumulated from 1999 would cost between US\$4.4 million (R63 million) and US\$8.2 million (R118 million).⁽⁵⁵⁾

1.9. Law governing disposal of medicine in South Africa

South Africa has a drug take-back or medicine return program that follows prescribed legal processes for the proper disposal of unused or expired medicines and hazardous chemicals.⁽³⁷⁾ The destruction of medicine can only take place in accordance with regulation 27 of the general regulations as published in terms of the Medicine and Controlled Substance Act 101 of 1965 (as amended), which states that no medicines and scheduled substances may be disposed of into the drain, refuse bin or municipal sewerage system. The destruction or disposal of medicine and scheduled substances must be done in such a manner as to ensure that it remains irretrievable. However these practices are seldom adhered to, with the exception of private hospital groups and government facilities. According to the South African Good Pharmacy Practice (GPP) rules, returned medicine remains the property of the patient, and even if the expiry date has not yet been reached, may not be re-used, re-sold or donated to poor countries or communities.⁽⁵³⁾

According to medicine and related substances control act 101 of 1965 regulations as per government gazette 41064 dated 25 August 2017, Schedule 5 and 6 may only be destroyed by a waste treatment facility authorised to destroy medicine or pharmaceuticals in the presence of an inspector, pharmacist or any other person authorised by the chief executive officer.⁽²⁵⁾ The waste treatment facility after the destruction of such scheduled medicine shall issue a certificate and maintain a record of the destruction carried out. The certificate issued must contain the name of medicine, quantity, date of destruction, names of all designated people who were present to witness the destruction process.⁽²⁵⁾

In South Africa, all collected pharmaceutical waste should be incinerated and a destruction certificate issued to the pharmacist as proof that such pharmaceutical waste has been destroyed in accordance with the GPP ⁽⁵³⁾ and local environmental health legislature (National environmental management: Waste Act 59 of 2008).⁽²⁵⁾ According to the Medicine and related substances control Act 101 of 1965 as amended, all medicine returned to a pharmacy for disposal should be recorded and segregated according to the dosage formulation. The destruction of medicine must be properly documented and the person responsible must date and sign off the destruction process. When a third party contractor is used, a destruction certificate should be issued.⁽¹⁾ Most of South Africa's privately owned pharmacies do not usually accept returned medicine from patients due to the high cost involved in the destruction process. According to A-Thermal Retort Technologies (a waste management and resource recovery facility located in Gauteng), the cost of medicine disposal in South Africa for 2017 was R15.90 per kilogram excluding logistic fees and tax.⁽⁵⁶⁾ With limited waste treatment facilities in South Africa, there is an added burden to travel to a state institution and the lack of knowledge on safe disposal and storage.

1.10. Disposal practices

Healthcare and pharmaceutical waste is considered the second most hazardous entity following radioactive waste according to the United Nations listing of hazardous and toxic materials.⁽⁵⁷⁾ Laws governing proper disposal practices are lacking in many African countries, and even if they exist, adherence is not in place. In those instances, where laws are lacking, the WHO's guidelines for safe disposal of unwanted pharmaceuticals should be followed to ensure the safety and protection of human health and the environment.⁽⁵⁵⁾

Acceptable disposal methods include the segregation of waste materials followed by encapsulation (immobilizing pharmaceuticals in a solid block within a steel or plastic drum), inerization (mixing of pharmaceuticals with cement or lime to form a paste), chemical decomposition (requires special chemicals and expertise for inactivation), and incineration at high (1200°C) and medium (850°C) temperature.⁽⁵⁵⁾

Some liquid pharmaceuticals, such as syrups and intravenous (IV) fluids, may be diluted with water and flushed into the sewers in small quantities over a period of time without serious public health or environmental affect, however this may have its disadvantages if not properly followed and supervised.⁽⁵⁵⁾ Unused or expired medicine marked for incineration are recorded in weight or volume. The accumulated medicine is not itemized in order to measure the value and amount, however records of the pharmaceuticals earmarked for incineration are kept by the requesting institution (pharmacy or hospital) and record maintained waste treatment facility. The frequency of medicine disposal depend on the volume or weight of the batch to be incinerated, resulting in periods characterized by low or high returns.⁽³¹⁾

1.10.1. Local trends

Studies conducted in Limpopo found that many health centers in the Polokwane municipality were disposing pharmaceutical waste improperly.⁽⁵⁸⁾ It was observed that most of these health centers and clinics did not segregate pharmaceutical waste from general waste, nor was this waste categorized according to dosage form as mandated by the law National environmental management: waste act 2008 (Act 59 of 2008).⁽²⁵⁾ The majority of clinics did not have an adequate storage facility for their medical waste.^(58, 59) In Kwazulu-Natal, it was found that pharmaceuticals were not disposed according to the regulation, but rather improperly disposed by dissolving and flushing down the drain or septic tank toilet. ⁽⁵⁹⁾ There was lack of knowledge concerning the transportation and handling of pharmaceutical waste. It was noted that clinics and health centers in that district had high numbers of needle prick and other occupational injuries due to negligence and disregard for occupational health and safety protocols.⁽⁵⁹⁾

1.10.2. International trends

Surveys conducted in the USA indicated that the most common methods of disposal of unused and expired medicine is discarding it in the trash (30%) and flushing down the toilet (26%).⁽³⁵⁾ In Australia, 67% stated that medicine were disposed in municipal bins together with household waste, 25% disposed medicine by flushing it down the

drain.⁽⁶⁰⁾ In Thailand, the most common method used by patients to dispose medicine was trashing it in refuse bins. Oral solid dosage forms (81.4%) followed by liquid oral dosage forms (64.6%) and medicine for external use (66.6%) were the most common medicine trashed in municipal refuse bins.⁽⁶¹⁾ It was reported that there was no significant difference between gender in respect to disposal practices.⁽⁶¹⁾ Washing expired medicine down the sink can result in a serious ecological concern, since this practice increase the load of chemicals into the recyclable waste water system.⁽⁶²⁾

Similar trends were found in Kuwait, where more than two thirds (76.5%) of patients threw medicine in a municipal trash bin, or flushed unwanted medicine (11.2%) down the toilet.⁽¹¹⁾ Another reported disposal mechanism included expired medicine being given to family or friends. Only 11.9% of patients returned medicine to the pharmacy.⁽¹¹⁾ Likewise, studies from Ghana and Kabul showed that more than half of the respondents were in possession of unused medicines, of which 75% and 77% respectively of these medicines were improperly disposed of in general refuse bins, destined for landfill sites.^(63, 64) The study also indicated that the majority of patients were unaware of the negative environmental impact and adverse effects on human health due to discarding expired pharmaceuticals in an unsafe manner. It is estimated that only 4% of the Ghanaian population disposes medicine by returning to the point of issue.⁽⁶³⁾

Eighty eight percent of people residing in Ireland kept unused medicine in their homes, of which 68% had done so for future use, should an ailment re-occur. Inappropriate disposal was observed in 72% of the participants in Ireland.⁽⁸⁾ Discarding as household waste (51%), and flushing down the sink (29%) and toilet (14%) was identified as the main methods of disposal.⁽⁸⁾

Countries like Egypt, Malaysia and India had used improper disposal practices such as ditching it in the municipal bin, flushing it down the toilet, or dumping it in a river or lake.^(47, 65, 66) In Sweden only 3% indicated that they discard unused medication in a bin, 55% stated that they saved medication for future use, and 43% claimed to return any unused pharmaceuticals back to the pharmacy.⁽⁶⁷⁾ In contrast to most other

countries that were surveyed, none of the Swedish respondents flushed medicine down the toilet. ⁽⁶⁷⁾ In New Zealand, most people (60%) accumulated expired solid dosage form medications such as tablets and capsules (13-24%) which were returned to the pharmacy for safe disposal.⁽¹⁵⁾ Liquid dosage forms were however more likely to be flushed down the toilet or poured into the kitchen sink.⁽¹⁵⁾

1.10.3. Medicine disposal by pharmacists

Improper disposal practices do not spare the pharmacist. In a study conducted by Tong *et al.* several community pharmacists in New Zealand were interviewed to assess their knowledge regarding the proper disposal of unused or expired medicine.⁽¹⁶⁾ Almost half of all pharmacists interviewed admitted to discard unused or expired solid dosage form (tablets) down the toilet or sink.⁽¹⁶⁾ This was more notable for the liquid dosage forms (suspensions/syrups), where 75% indicated that pouring it down the drain was common method of disposal.⁽¹⁶⁾ Only 23% of pharmacists used third party contractors to dispose of medicine returned by patients. Of these pharmacists, 62% were aware that the collected pharmaceutical waste were destined for incineration, while almost a quarter had no knowledge on how the contractors disposed of the waste being handed over to them.⁽¹⁶⁾

1.11. Consequences of improper disposal practices

Having unused and expired medicine stored improperly at home can present an added risk of accidental poisoning by children, or intentional poisoning by adults. Not only does the accumulation of medicine have a significant financial burden on the healthcare budget, but improper disposal practices may cause harm to the environment and community members.⁽¹²⁾ Calculating the true cost of unused and expired medicine should include the additional unnecessary expenses associated with the damage to the environment, including hospitalization as a result of unintended poisoning from ingesting improperly discarded medicine. A possible solution to reduce the environmental burden, is to prioritize and provide education concerning safe disposal methods of expired and unused medicine at the time of dispensing.⁽¹⁷⁾

1.11.1. Air pollution

The inadequate incineration of pharmaceuticals at very low temperatures or in open domestic flames may lead to the release of toxic pollutants into the environment with unintended consequences.^(55, 68) Burning pharmaceutical waste in an open flame at low temperature is not advocated as a method of disposal.⁽⁵⁵⁾ Many clinics and health centers in the greater Polokwane municipality were found to be burning pharmaceutical and medical waste in open fire-pits, potentially leading to air pollution.⁽⁵⁸⁾

The method used to dispose medicine was largely dependent on the medicine dosage form and the available financial resources in a particular area. In Lithuania, it was reported that 50% of residents burn medicine in their backyards.⁽¹⁸⁾ The practice of burning unused medicine with the rest of household waste was also reported in Ghana (>10%),⁽⁶³⁾ and Nigeria (9.9%)⁽¹⁴⁾. This practice is observed in many rural areas of South Africa, and is reported to have a negative effect on the ozone layer, which in addition may contribute to global warming and local environmental pollution.^(18, 58, 59)

1.11.2. Contamination of water sources

The presence of pharmaceutical compounds in drinking water has been associated with incorrect disposal of medicines which is evident from studies conducted in Sweden,⁽¹²⁾ USA,^(62, 69) Asia, Australia, Canada, Europe⁽⁷⁰⁾ and South Africa.^(71, 72) Pharmaceuticals (prescription and over the counter medicine) have been detected in water storage systems. Several ways in which pharmaceuticals end up in drinking water have been identified.^(70, 73, 74) The unavoidable contamination of water sources by pharmaceutical active ingredients, as a result of unchanged metabolite excretion, is by far less significant than improper disposal practices such as flushing it down in the sewerage system, which has a direct impact on the water environment.^(17, 75) Other methods of water contamination may be directly linked to inappropriate disposal practices from pharmaceutical manufacturing companies or hospitals.⁽⁷⁰⁾

There is a need to explore and reduce the quantity of chemical waste produced and discarded during the manufacturing of pharmaceutical compounds. Although stringent guidelines exist for dealing with chemical by-product produced during the manufacturing process, these processes are not always adhered to, and often result in the contamination of water sources.⁽⁷⁶⁾ Albeit water for human consumption are exposed to water treatment and purification plants before being integrated into the water-supply systems, it has been reported that these “clean water sources” still contain pharmaceutical contaminants.⁽⁷²⁾ Certain advanced water treatment methods with membrane to further reduce pharmaceutical contamination of water sources such as microfiltration, membrane bioreactors prior to reverse osmosis. does exist, however the cost of these procedures are unjustifiably high and therefore alternative methods needs to be developed and explored.^(77, 78)

From the literature reviewed, it was only reported in Sweden and Lithuania, that none of the residents flushed unused or expired medication down the toilet.⁽¹⁸⁾ This results may have been due to the unavailability of a working sewerage system or septic tank in Lithuania.⁽¹⁸⁾ From observation, most households in Gauteng have running water, proper sanitation and functioning sewerage systems except in the informal settlements where available sanitation is through the bucket system or communal toilet facilities.

A study conducted in the Umgeni River water system in Kwazulu-Natal found high concentrations of antibiotics, antipyretics, atenolol, bezafibrate and caffeine in wastewater and surface water samples from the Umgeni river.⁽⁷¹⁾ Water analyzed after going through the treatment process at the plant showed a reduction of between 43-94% for most chemicals, except for atenolol, which only showed a reduction of 18%.⁽⁷¹⁾ In another South African study conducted in the Kwazulu-Natal Msunduzi river, nalidixic acid was among the top antibiotics identified in populated urban city centers, whilst aspirin was found to be in high concentrations in rural and sub-urban areas.⁽⁷²⁾ The concern however remains that these purification processes

does not remove 100% of all the pharmaceuticals and still end up contaminating some of the drinking water.⁽⁷¹⁾

The risk posed by improper disposal of medicine is that people might be affected by long term exposure to low amounts of pharmaceuticals in recycled drinking water.⁽⁶⁹⁾ Unfortunately, no long-term quantitative study to date has been able to conclusively elucidate the adverse effects in any population exposed to such conditions.⁽⁷⁰⁾ Similarly, no regulatory limits regarding pharmaceutical active ingredients in drinking water has been established in South Africa. Allergic reactions, antibiotic resistance, and hormonal imbalances may occur from consuming pharmaceuticals present in drinking water.⁽⁶⁹⁾ It remains difficult to predict the likelihood of occurrence of the allergic reaction because reaction may occur at a very low concentration depending on sensitivity of individual.⁽⁶⁹⁾ The increase demand for fresh water, compounded by drought in many parts of the world, including South Africa, may possibly lead to a higher incidence of exposure to pharmaceuticals through recycled drinking water sources.⁽⁷⁸⁾

1.11.3. Diverted for re-sale, abuse or re-use

Improper disposal of unused or expired medicine, in particular opioid analgesics, may lead to illegal drug diversion or abuse.⁽⁵⁴⁾ A rising trend among the impoverished youth in some South African communities is combining narcotics with other pharmaceuticals for recreational purposes. A study conducted by *Gretotti et.al* showed that some patients collected their ARV's for resale and manufacturing of street drugs "nyaope" or "whoonga", thus adding to the rising cost of medicine expenditure.⁽⁷⁹⁾

Studies conducted in New Zealand found that benzodiazepines, methylphenidate and anabolic steroids, were reported among the top abused pharmaceuticals for recreational use. Steroids were reported to have scored high on physical harm.⁽⁷⁵⁾ Many countries donate unusable stock to poor communities mainly to avoid the cost of proper disposal.⁽⁸⁰⁾ Such practice leave the poor communities with multitudes of

problems ranging from antibiotic resistance, abuse, poisoning and environmental contamination.⁽⁸⁰⁾ Studies conducted in India, indicated that 2.1% of patients donated unused medication to hospitals, pharmaceutical companies and non-government organizations for re-use.⁽⁸¹⁾

Between 27 800 to 34 800 tons of medication were donated to Bosnia and Herzegovina between 1992 and 1996.⁽⁸⁰⁾ Three categories of donations were identified, each one involving some degree of inappropriateness. One of these donations conformed to the WHO guideline for drug donation and such consisted of hospital packs containing a single drug relevant to the disease pattern of the recipient country.⁽⁸⁰⁾ Packs that were clearly labeled and having a remaining shelf life of at least one year was accepted. Only 5% of these donations were found to be inappropriate for human consumption.⁽⁸⁰⁾

Another type of donation included miscellaneous drugs collected from health professionals, private homes and charity organizations, however 90% were considered inappropriate for human use for various reasons (unlabeled, expired, unsorted).⁽⁸⁰⁾ The third type included large quantities of useless and undesirable medicine, mostly from army supplies dating back to World War II. In total, around 60% of all donated medicines were considered inappropriate, however at the time Bosnia accepted all these donations.⁽⁸⁰⁾ The implication thereafter resulted in added healthcare costs, environmental hazards and the cost of storing, handling, sorting and disposing of these unusable medicines.⁽⁸⁰⁾

Different views about medicine re-use however exist. Studies conducted in the Netherlands found that many respondents felt that re-dispensing of medicine can save cost.⁽⁵⁰⁾ However there is a common agreement that the quality of returned medicine should be guaranteed before medicine can be re dispensed.⁽⁵⁰⁾

According to a study conducted in the UK by Mackridge *et al.* ⁽³⁹⁾ the researchers suggested that almost one third of medicine returned from patient`s homes could be re-used, thereby reducing the large number of pharmaceuticals being wasted. Their conclusion was based on the WHO guidelines regarding medication re-use. These included the listing as an essential drug, adequate labelling and still within the expiration date. It was nonetheless acknowledged that unknown storage conditions, at patient`s home exposure to high humidity and temperatures, and physical handling of medication may present with unintended challenges such as toxicity or ineffective treatment.⁽⁵²⁾

1.11.4. Poisoning

The inappropriate storage and accumulation of unused or expired medicine in households may lead to accidental ingestion or intentional abuse or suicide.⁽⁸²⁾ Poison information centers around the world are inundated by calls from family members and care givers seeking advice on medicine overdose.⁽⁸³⁾ According to the United Nations Children`s Fund (UNICEF), 45 000 children and young adults died as a result of poisoning during 2004.⁽⁸⁴⁾ Poisoning is reported to be among the top four causes of accidental injury in high and middle income countries for this population group.⁽⁸⁴⁾

Sensory curiosity and the will to explore their environment are postulated as being some rationale for the high incidence of poisoning in children under the age of one year.⁽⁸⁴⁾ The number peaks again at the age of 15 years due to the experimental adolescent stage.⁽⁸⁴⁾ Boys are more prone to poisoning compared to girls, mainly due to different ways in which different genders socialize.^(82, 84) In addition, boys tend to engage in high risk behavior, whilst girls are more likely to practice caution with certain behavior.⁽⁸⁴⁾ In the United Kingdom, more than 90 000 cases of poisoning caused by medicine, requires hospital admission every year.⁽⁸⁵⁾

Children below the age of five years are more prone to accidental poisoning from chemicals or medicine (prescription or over-the-counter), as a result of curiosity and

poor storage practices. Aspirin, vitamins, iron supplements, antihistamines and paracetamol are notorious contributors of accidental poisoning in children.^(84, 86) A recent study conducted in Gauteng demonstrated that 17% of pediatric hospital admissions were as a result of accidental poisoning.⁽⁸⁷⁾ A study done in Botswana also confirmed that boys were more affected by poisoning than girls.⁽⁸⁸⁾ Most of the poisoning admissions were the result of oral ingestion. The average cost of treating a poisoned patient is approximately R617.24 per day, with an average hospital stay of 2 days for South Africa, Botswana and Uganda.⁽⁸⁸⁾

According to Maharana *et al.*⁽²⁵⁾ none of the respondents in a study conducted in west Bengal practiced safe storage. About 16.7% had stored medicine within reach of children.⁽⁶⁵⁾ In Saudi Arabia some families stored medicine in the car where the temperature is uncontrolled.⁽³⁾ Poisoning from pharmaceutical substances in adolescents and adults globally, are mostly the result of intentional ingestion or attempted suicide.⁽⁸⁹⁾ In the USA, prescription opioids used in pain management are responsible for more fatalities than illegal narcotics.⁽⁵⁴⁾ A survey conducted at the Tygerberg poison information center reported that 65.2% of poisoning cases were as a result of accidental ingestion, while only 34.8% were due to intentional or attempted suicide.⁽⁸²⁾ The most common reported medicine responsible for poisoning were antihistamines, benzodiazepines and analgesics.⁽⁸²⁾

1.12. Study aim

The aim of this study was primarily to determine what proportion of patients return unused and expired medicine to the Steve Biko Academic Hospital (SBAH) pharmacy and to determine the reasons for unused and expired medicine being returned.

1.13. Study objectives

1.13.1. Primary objectives

1. To determine the demographics and proportion of patients that return unused or expired medicine to a tertiary academic hospital pharmacy in Gauteng.

2. To determine the reasons for unused and expired medicine being returned.
3. To determine the cost, type and quantity of unused and expired medicine returned.

1.13.2. Secondary objectives

1. To assess the knowledge of the study population regarding the procedures in disposing unused and expired medicine.
2. To determine and identify the reasons patients accumulate unused or expired medicine.
3. To determine the different practices of the study population in disposing unused or expired medicine.

Chapter 2: Methods and study design

2.1. Study design

This was a cross sectional, descriptive observational study where the researcher administered a semi-open ended questionnaire to patients who visited SBAH to either collect their monthly prescription for chronic use, and/or return unused or expired medicine back to the pharmacy for disposal.

2.2. Setting

The study was conducted at SBAH pharmacy. SBAH is the second largest urban tertiary hospital pharmacy in Gauteng servicing residents from the Tshwane metropolitan area.

2.3. Patient/research object selection

Probability sampling was used as a sampling strategy. A “Drug take-back or medicine return program” was initiated by displaying posters at strategic locations at SBAH. These included the pharmacy, various clinics, out-patient departments and in the hospital wards. Daily institutional announcements of the “Drug take-back or medicine return program”, including information sessions aired on two local radio stations (Pheli FM and TUKS FM) three weeks prior to, and during the data collection period (6 March – 17 March 2017) were made. These information sessions and posters were used as a recruitment tool for prospective participants (patients, family members and care givers over the age of 18 years) to return any unused or expired medicine to pharmacy. Only medicines for human use were included in the study.

The researcher, (a registered pharmacist with the South African Pharmacy council), performed all patient interviews and collected all medicine returns personally. No data collection was delegated to other individuals employed at the pharmacy. All patients who returned medicine or those who attended the pharmacy to collect their medicine were invited to partake in the study.

The researcher explained the study aim and objectives to potential participants and only after completing a signed patient or participant's information and consent form (Appendix 1) was the questionnaires (Appendix 2) administered. Participants' personal details and identifiable information were not recorded.

All participants were given the assurance that questionnaires were completed anonymously, and data collected could not be used to trace them down. No entry in their patient records were made to indicate that they participated in this study. Patients were not penalized or negatively affected by their participation, nor were they remunerated for their efforts.

2.3.1. Questionnaires

Participant responses to the research questions were captured and recorded as stated by the researcher. Questions included reasons for medicine return, storage, disposal practice during the past year, previous history or poisoning incident at home, knowledge regarding the cost of medication being dispensed, the type of medicine including the condition for which it is prescribed, and if prescribed antibiotic or analgesic treatment was completed. (Appendix 2)

2.4. Measurements

Demographical data (age, sex and race) was collected for statistical purposes. The objectives of this study were achieved by exploring the following variables:

- The proportion of patients that returned medicine
- Demographics of respondents who returned unused or expired medicine
- Why medicines were returned to SBAH
- The cost of returned medicine
- Type of medicine returned
- Number of returned medicine and dosage form

- Pharmacological classification of medicines returned
- Usual medicine disposal practice
- Knowledge regarding proper medicine disposal

Descriptive statistics were used to categorize the above variables according to the demographic profile and to estimate the proportion of the population who returned unused and expired medicine in each reason category. A cost calculation for each returned drug-group was done.

2.5. Statistical consideration

All statistical analysis, including sample size calculation, was supervised and checked by Prof Piet Becker, a biostatistician allocated to the Faculty of Health Sciences, University of Pretoria. (Appendix 3)

2.5.1. Sample size

A convenience sample size of at least 97 completed questionnaires were required to estimate the proportion of patients that returned medication to an accuracy of within 0.1 (10%) with 95% confidence. The sample consisted of patients attending the SBAH pharmacy who had consented to partake in the study, either collecting their monthly prescription or returning unused or expired medication.

2.5.2. Data analysis

The proportion of patients who returned medicine for safe disposal and reasons put forward by respondents were assessed. Furthermore, confidence interval for proportion was also explored. Visual representation of data collected was in the form of tables. A total of 127 completed questionnaires were collected, after which they were sorted and individually coded. The data was entered into a password protected Microsoft Excel spreadsheet. Statistical Analysis System (SAS) version 9.4 software was used for data analysis. The monetary value of all expired and unused medicines received was recorded and calculated using the current pricing structure on tender.

The value of returned medicine was calculated according to the number and type of tablets or capsules received. Liquid dosage forms were calculated as a full bottle and creams as full tube. All returned medicine was categorised according to their pharmacological classification indexed in the South African Medicine Formulary (SAMF).

2.6. Ethical considerations

Ethical approval for this study was obtained from the Faculty of Health Sciences Research Ethics Committee (FHSREC) of the University of Pretoria (Ref 19/2017) (Appendix 4), following project approval by the MMed scientific committee (Appendix 5). All the required consent forms and questionnaires were constructed in accordance with the FHSREC regulations.

Written patient or participant informed consent was obtained prior to participants being interviewed by the principal investigator. Participation was voluntary, and participants were assured of their confidentiality. Participants were assured that they may withdraw from answering the questionnaires at any moment, without the need to give an explanation. Questionnaires did not contain any identifiable information, only questionnaire numbers were captured. Participants were not refunded for any medicine being returned, nor for their participation in the study. This study did not influence or compromise any treatment that the patients were receiving from pharmacy or clinic.

Chapter 3 – Results and discussion

3.1. Patient demographics

Patient demographics included general characteristics such as race, gender, age distribution and the person responsible for completing the questionnaire (Tables 1 and 2). Economic status and level of education was not assessed, however through personal interaction it was evident that most respondents had little or no education and only knew how to write their name. There was a female predominance (57.5%), and most participants were black (69.3%). This observation is in contrast to a similar study conducted in Afghanistan, where participation showed a male predominance (73.4%) compared to female 26.6%.⁽⁶⁴⁾ Ages between 18-20 had 1 male and 3 females, 21-30 (6 male and 10 females), 31-40 (9 male and 16 females), 41-50 (12 male and 15 females), 51-60 (10 male and 17 females), 61-70 (12 male and 8 females) and 71-80 (4 male and 4 females).

It was found that the age groups between 41-60 years accounted for more than 40% of the study population, and accounted for most of the chronic medicine being returned. Ages between 41-60 and 71-80 years returned 10 and 5 chronic medicine packages respectively. The age group between 21-50 years accounted for 80% of returned acute medication. In comparison to a study conducted in Sweden, medicine returns between 30 September and 04 October 2003, reported 8795 medicine packs being returned from 59 community pharmacies (average of 149 medicine packs per pharmacy).⁽¹²⁾ Another study conducted in New Zealand also showed a higher amount of returned medicine (1605 medicine packs) in the four week study period. Forty percent of the returned packs were from the age group 61-80 years, whereas the group between 41-60 years in the current study amounted to the equivalent of 40%.⁽¹⁰⁾ It is evident that medication returns in the SBAH is significantly less than what is reported in similar international studies.

Table 1. Race and participants who completed questionnaire

	Responsible for completing questionnaire			Race			
	Care giver	Family	Patient	Black	Coloured	White	Other
Frequency (n)	8	9	110	88	25	9	5
Percentage %	6.3%	7.1%	86.6%	69.3%	19.7%	7.1%	3.9%

Table 2. Gender and age distribution of participants

	Gender		Age distribution						
	Male	Female	18-20	21-30	31-40	41-50	51-60	61-70	71-80
Frequency (n)	54	73	4	16	25	27	27	20	8
Percentage %	42.5%	57.5%	3.1%	12.6%	19.7%	21.3%	21.3%	15.7%	6.3%

3.2 Type of medicine usage

3.2.1 Analgesic use

Half of the respondents n=64 were currently taking pain medicine. There was female predominance at ages between 31 and 60 years while male predominance was evident between 41 and 70 years. The most commonly used analgesics included tramadol and paracetamol, either alone or in combination. When asked if they would complete the prescribed treatment, 51.6% (n=33) indicated that they intend to complete the course. The remaining respondents (48.4%) not willing to attain completion indicated that they would only use prescribed analgesic when necessary (Table 3). This was consistent with review studies done in the USA in 2017. About 67 to 92% respondents reviewed from six studies indicated that they had unused opioids. Several reasons for unused analgesics were identified, which included patients only taking medicine when pain control is needed, and avoidance of these agents due to adverse effects.⁽⁹⁰⁾

Table 3. Reasons for not completing pain medication

	Frequency(n)	Percentage
Used to manage pain when needed	27	64.3%
No reason given	15	35.7%
Total	42	100%

3.2.2. Antibiotic, antifungal and antiviral use

From all of the respondents who participated in the study, 4.7% were currently taking antibiotic/antiviral or antifungal agents for various infective conditions. The age group consisted of 4 males and 2 female at the ages between 21 and 60 years. Some of the respondents did not know the condition which the medicine were used for. All respondents n=6 who were on antifungal, antiviral and antibacterial medication indicated that they would complete the full course of treatment and realized the importance of completion. The low number of respondents taking antifungal, antiviral or antibiotic agents was not sufficient to make a conclusion regarding treatment adherence.

3.3. Returned medicine

The proportion of patients who returned unused or expired medicine to tertiary academic hospital pharmacy was twenty-five respondents (19.6%) during the two week "Medicine take back or medicine return" program. A total of 34 medicine packets were returned, averaging a rate of 3.5 packs per day, and 1.4 packs per patient. Of all returned medicine, 24 items (70.6%) were classified as chronic medicine and 10 items (29.4%) were regarded as acute medicine. (Table 4). Oral solid dosage formulations (tablets and capsules) were in the majority of returned medicine n=488 followed by Insulin pens, liquid oral medicine, spray canisters n=2 respectively and lastly cream ,bag of compounded medicine n=1. 88% were patients returning their own medicine while 8% and 4% were family members and care givers returning medicine for adult patient and children respectively.

The majority of respondents returning medicine to the pharmacy were between 41-50 years with a mean age of 47.3 years (SD ± 15.22 years). Ages between 51-60 years followed by 41-50 and 71-80 respectively returned most chronic medicine and ages between 41-50 followed by 21-40 returned most acute medicine. Seventy six percent of females returned medicine, of which 60% were acute and 79% were chronic. Twenty four percent of male participants returned medicine where 40% were regarded as acute and 21% as chronic medication.

All returned medicines were evaluated according to the pharmacological classification and type of dosage form. Liquid medicine, insulin pen, spray and creams were regarded as a full container, and not according to the actual quantity returned. Tablets and capsules were calculated according to the actual quantity of the dosage form being returned. The monetary value of all returned medicine by patients during the two week collection period was determined to be R652.11 (Table 4). Chronic medicine contributed R586.59 while acute medicine contributed R65.52. This value did not include any medicine that was returned from wards or expired in the pharmacy.

Table 4. Type and value of returned medicine

Medicine type	Frequency(n)	Value in ZAR	Percentage
Chronic	24	R586.59	70.6%
Acute	10	R65.52	29.4%
Total	34	R652.11	100%

The quantity of returned medicine was less compared to pharmacy statistics from the previous year, where an average of 9 packs returned per day was recorded. A sundry of reasons could be responsible for the low medicine return rate despite the campaign inviting patients and members of the public to participate. The reason for low turnout of respondents is unknown. It could be possible that individuals may not

have realized the importance of participating in the study and proper disposal practices and decided to continue using unwarranted methods such as flushing down the toilet or sink, or simply discarding medicine together with household trash. About 41% of medicine returned had more than 50% of the original amount of medicine dispensed.⁽¹³⁾ Most returned medicines in this study were Prexum (perindopril), insulin and metformin.

It could be possible that the socioeconomic status of potential participants relying on the public healthcare system could have prevented them to incur additional travel expenses to attend the hospital when not for their own personal benefit. It seemed likely that these healthcare users would rather return unused medicine at the time scheduled for their follow up consultation, or when a medicine refill was required. The short duration of data collection period could therefore have limited the participation. Patients might additionally have been hesitant to participate in such a study out of fear of being reprimanded for harbouring expired medicine or accumulating prescription medicine. Other studies conducted around the world had longer duration compared to this study and had multiple drop off and participation areas. This study had one location for return and interviewing of participants.

In contrast to Kuwait and Jordan where most chronic medicine may be obtained from private pharmacies without a prescription, (except narcotics and major tranquilizers^(11, 91, 92)), most chronic medicine in South Africa are classified as schedule 3 substances and above, and therefore require a prescription before it may be dispensed. The medicines and related substances control act 101 of 1965 however makes provision for patients who are responsive to treatment and does not require monthly follow up assessment to receive a six-month prescription dispensed monthly at a hospital pharmacy, down referral clinic or CCMDD pickup point without consulting the doctor. Despite this legislative provision, large numbers of patients who are responsive to treatment and do not require monthly follow up assessment still make use of the tertiary hospital to collect their chronic monthly prescriptions, placing unnecessary strain on the overburdened health system. It could be that

these patients often perceive tertiary hospital services as being superior to regional, district and local healthcare centres.

3.4. Pharmacological classification of returned medicine

As outlined in Table 4 above, 70.6% of all returned medicine were considered to be used in the management of chronic diseases, while 29.4% were used for acute treatment. Most were analgesics used in the management of pain. Ages between 21 and 50 years had more returns of acute medicine. More than a third (37%) of the interviewed participants indicated current use of medicine for various chronic conditions. These included hypertension, diabetes mellitus, asthma, tuberculosis, HIV, depression, anxiety, heart failure, renal failure and cancer. Cardiovascular disease (hypertension, diabetes and heart failure) was predominant. This correlated with the type of medicine returned for use in the treatment of cardiovascular diseases.

Pharmacological classification of returned medicine corresponded with the cited conditions by interviewed participants. Cardiovascular agents were among the top together with, anti-diabetic drugs, respiratory drugs and corticosteroids each contributed 11.8% to the returned medicine packets (Table 5). Studies around the world widely reported that cardiovascular medicine were among the top returned medicine by patients.^(9, 13) Respiratory agents were reported as the second most returned medicine apart from cardiovascular agents.⁽¹³⁾ This correlate with the study review conducted in Australia where top prescribed medicine in 2016 were chronic cardiovascular agents.⁽⁹³⁾ The comparison of commonly prescribed and dispensed medicine to returned unused or expired medicine was not done. In another study cardiovascular agents came out second to gastrointestinal agents.⁽⁴⁴⁾ The remaining 52.8% of returned products consisted of analgesics, anti-epileptics, ARV's, psycholeptic agents, antihistamines, non-steroidal anti-inflammatory agents, musculo-skeletal agents, vitamin and mineral supplements, anti-anaemic drugs, immunosuppressants, antibiotics, anti-thrombotic agents, alkalinizers and urological preparations.

Table 5. Pharmacological classification of returned medicine

	Frequency(n)	Percentage
Cardiovascular agents	4	11.8%
Anti-diabetes agents	4	11.8%
Respiratory agents	4	11.8%
Corticosteroids	4	11.8%
Anti-epileptic agents	3	8.8%
Analgesics	2	5.9%
Antiretroviral agents	2	5.9%
Anti-anaemic preparations	1	2.9%
Immunosuppressants	1	2.9%
Antibiotics	1	2.9%
Anti-thrombotic agents	1	2.9%
Alkalinizers	1	2.9%
Non-steroidal anti-inflammatory agents	1	2.9%
Urological agents	1	2.9%
Psycholeptic agents	1	2.9%
Antihistamines	1	2.9%
Musculo-skeletal agents	1	2.9%
Vitamin and mineral supplements	1	2.9%
Total	34	100%

3.5. Reasons for medicine return

A summary of the reasons unused and expired medicine were returned to the pharmacy are listed in Table 6 below. The principal reasons for return was that patients felt better resulting in self-discontinuation, or they were non-adherent to prescribed treatment (36%). The same reasons were recorded for 67% of returned over-the-counter products. Discontinuation of treatment by prescribing doctor accounted for (16%) of medicine being returned. This reason contributed to the high number of cardiovascular medicine being returned.

The remainder cited undesirable side effects (12%), over supply (12%), death of a family member/patient (8%),⁽³¹⁾ incorrect medicine supplied (4%), medicine duplication between the public and private sector (4%), and a short expiry date (4%) as additional variables. The remaining (4%) did not know or did not provide reasons for returning unused medicine. Over supply and incorrect medicine supplied contributed to high corticosteroids and anti-diabetic agents respectively being returned. It was noted in a review study in 2017 that most patients who were using prescription opioid analgesics after surgery stopped using once pain had subsided while some discontinued using opioids analgesics due to undesirable side effects.⁽⁹⁰⁾

Table 6. Reasons for expired and unused medicine returned

Patient response	Frequency(n)	Percentage
1.Felt better /non adherence	9	36.0%
2.Doctor discontinued treatment	4	16.0%
3. Undesirable side effects	3	12.0%
4. Over supply	3	12.0%
5. Patient passed away	2	8.0%
6. Incorrect medicine supplied	1	4.0%
7. Short expiry of compounded medicine	1	4.0%
8. Unknown	1	4.0%
9. Duplication from public and private	1	4.0%
Total	25	100%

A worrying observation was the large amount of patients discontinuing their treatment without consulting a healthcare professional, which constitute non-adherence. Non-adherence to prescribed treatment in this study population needs to be addressed and patients educated on the importance of adherence to reduce medicine wastage. Majority of patients discontinuing treatment when feeling better were using medicine for acute treatment. Comparative studies conducted in Saudi Arabia and Lithuania reported accumulation and expiry of medicine as a result of non-adherence to be approximately 25% and 36.4% respectively.^(3, 43) The majority of females (62.5%) in this study were not adherent to their treatment but in a study conducted in Lithuania found that there was no significant difference in adherence between males and females.⁽⁴³⁾ Other studies correlating with our findings were conducted at the University of Oklahoma, where 60% indicated that they discontinued treatment because they felt better.⁽⁴⁶⁾ In Sweden, discontinuing medicine use because of an improvement in the condition was recorded among the top three reasons why medicine was unused.⁽¹²⁾

The rational use of medicine requires a patient to receive treatment which is appropriate for the intended condition, adjusted to their individual requirements, for an adequate period of time, and at an affordable cost to the funders.⁽²⁸⁾ This may come at an extra financial burden to the patients.⁽⁴⁵⁾ Non-standardized packaging of medicine by manufactures further contributes to an unintended accumulation and expiration of medicine. Many government institutions issue original packaging that contains a supply of 28 calendar day treatment, while others have a 30 calendar day quantity. Patients receiving both 28 day and 30 day calendar packs will accumulate an additional month's supply after a period of 15 months, which may ultimately be discarded or inappropriately diverted or returned to pharmacies, contributing to wastage. NHS was encouraged to reduce dosage units to a 28 day supply due to the literature on wastage and cost of wasted medicine.⁽³²⁾ In Portugal, the cost of medicine associated with different pack sizes dispensed to the same patient at the same time was estimated at an average of €1.75 (R26.00).⁽⁴⁾

The issuing of incorrect medicine or wrong dosages to patients attending down referral clinics are becoming a challenge and are counterproductive in efforts to minimize medicine wastage and overcrowding at district, regional and tertiary academic hospitals. It has been observed that primary healthcare nurses are overburdened with clinical work, and often lack appropriate pharmaceutical training on the correct handling and dispensing of medicine. The requirements of an ideal clinic, as outlined in the NHI white paper, calls attention to the employment of pharmacists, or post-basic pharmacist assistants acting under indirect supervision of a pharmacist, to ensure that adequate pharmaceutical services are delivered to primary healthcare centres.⁽⁹⁴⁾

Duplication of treatment from both public and private facilities is of serious concern as it may result in potential overdose or medicine accumulation. Products obtained from private institutions often have different trade names to state issued medicine. Although these products contain the same pharmaceutical active ingredient, it is assumed that patients are unaware of the similarity. It is speculated that many

patients utilizing both private and public institutions believe that the public sector hospitals are incapable of providing high quality treatment and pharmaceutical care. Because of patient's lower socio-economic status, it is assumed that these patients remain in the public sector but will access private healthcare when they can afford to do so. Proper history taking regarding chronic medicine use is consequently not performed, which result in treatment duplication and medicine accumulation. It was noted in studies conducted in Oman, where switching from one public hospital to another or multiple visit to the same hospital by patient was one phenomenon associated with the supply of free medicine.⁽⁹⁾

The proposed NHI is designed to address the differences present in the quality of healthcare between the private and public sector healthcare facilities. Implementation of the NHI will aim to equip public facilities to render pharmaceutical services at a level equivalent to that experienced in the private sector, as defined in section 27 of the constitution.⁽⁹⁴⁾ The use of integrated computer systems detailing a patient's medication and treatment history may address some of the factors responsible for treatment duplication between facilities. Medicine accumulation and wastage may therefore be reduced by adequate information-technology systems. It has been reported in other studies in South Africa that patients visit multiple health facilities to obtain antiretroviral medicine for the purpose of manufacturing street drugs like Whonga, Nyaope etc. ⁽⁷⁹⁾

3.6. Storage of expired medicine at home

A third of the respondents (34.7%) indicated having expired medicine at their homes. The latter were stored in improper locations ranging from the bathroom cabinet, kitchen cupboards, dining room cabinets and bed dressers.

Fifty percent indicated that medicine were stored in their bedrooms where it was kept out of reach of children but not locked. The storage locations identified in this study were not unique and coincide with trends reported in previous similar studies around the world. However, none of the respondents indicated that they stored medicine in vehicles, as was reported in a study from Saudi Arabia.⁽³⁾

3.7. Methods of medicine disposal

Almost 77% of all discarded medicine from patient's home were done so by various unsafe methods. Based on responses obtained from this study, the act of disposing unused and expired medicine in refuse bin with other household waste was widespread. This practice was noted in 34.1% of participants who indicated that they had unused or expired medicine in the past 2016. This finding is contrary to the study conducted in Australia, where 60% indicated that they had unused or expired medicine.⁽⁶⁰⁾ The results of this study were consistent with the study conducted in Thailand and Afghanistan where most of the medicine were discarded by throwing in refuse bin^(61, 64) and in Thailand oral dosage forms contributed 81.4% of all discarded medicine.⁽⁶¹⁾ Discarding pharmaceuticals in the trash is a global phenomenon. As mentioned in chapter 1 section 1.11.2 above, similar studies conducted in Europe,⁽¹⁸⁾ West Bengal,⁽⁶⁵⁾ the Saudi Arabia, Kabul⁽⁶⁴⁾ and other Gulf countries,⁽¹¹⁾ New Zealand⁽¹⁵⁾, Australia^(60, 93) and other African countries such as Ghana⁽⁶³⁾ and Nigeria confirm this statement.⁽¹⁴⁾

Other disposal practices included flushing down the toilet or kitchen sink, burying it in a hole, or storing it for future use (Table 7). Only 13.6% of the respondents indicated that they would return expired medicine back to the pharmacy for safe disposal. This statement appears to be valid, since the actual amount of both expired and unused medicine returned during the collection period was calculated to be 34 medicine packets. It may therefore be concluded that approximately 6% of all returned medicine was still within the expiration date. In Australia only 17.6% were aware that medicine can be returned to pharmacy for safe disposal, which correlates with our finding of local respondents indicating to return medicine back to the pharmacy.⁽⁶⁰⁾ Table 7 below summarises the number of participants who have engaged in one of the listed disposal methods in the past.

Table 7. Methods of medicine disposal used in 2016

	Frequency	Percentage
Threw in municipal bin	15	34.1%
Flushed down the toilet	17	38.7%
Returned to the pharmacy	6	13.6%
Threw in a pit toilet	2	4.5%
Discarded into the drain	2	4.5%
Dug a hole	1	2.3%
Stored for future use	1	2.3%
Total	(n)44	100%

Respondents were asked specific reasons for engaging in these diverse disposal practices and methods. The majority (45.4%) believed that their chosen method was the most appropriate to ensure the safety of their children. Other reasons included the unavailability of alternative methods (4.5%), it was the only method known to them (25%), it was the safest method of disposal (13.7%), to ensure that expired medicine are not used again (4.5%), and to ensure the medicine was not identifiable (2.3%). The results from our study is similar to that of a study conducted by Oklahoma university, in which respondents rated the importance for the reason to return unused or expired medicine to pharmacy for safe disposal as being the safety of children at home.⁽⁴⁶⁾

Unsafe disposal practices may result in many challenges such as accidental or intentional poisoning at home. Four respondents reported incidents of poisoning, of which 3 (aged 5, 18 and 55 years) had been accidental poisoning. Intentional poisoning was only recorded in one female patient aged 15 years. From these responses it was evident that there was lack of knowledge regarding proper disposal practices among the study population. Participants seemed to be aware of the

dangers expired medicine may pose to their children, however extensive education on the correct disposal and destruction processes are required. In addition, all respondents were asked about their likelihood of discarding medicine in the municipal refuse bins, or flushing down the sewerage system (Table 8).

Table 8. Probability of discarding unused medicine in refuse bin or sewerage system

Response	Frequency(n)	Percentage
Uncertain	2	1.5%
Less likely	33	26.1%
Very likely	87	68.5%
No response	5	3.9%
Total	127	100%

More than two thirds (68.5%) of respondents indicated that they were very likely to dispose unused medicine in municipal refuse bins destined for landfill sites, or flushing down the toilet. Seventy seven percent of the respondents who indicated having unused or expired medicine in 2016, reported that they would most likely discard medicine by flushing down the toilet, drain or throwing in refuse bins. This practice correlated with the responses given in question 7 of the questionnaire (appendix 2) where 77% of respondents indicated that in 2016 they had discarded unused or expired medicine in refuse bins or by flushing down the toilet or drain. Of all those who indicated that they returned medicine to pharmacy for safe disposal in 2016 their response stated that they were less likely to discard unused or expired medicine by flushing in toilet and drain or by throwing in municipal refuse bin. Their responses corresponded with the answers given in the assessment of the study population regarding the knowledge on proper disposal of unused or expired medicine (Table 8).

The majority of respondents indicated that the motivating factor to throw unused or expired medicine in refuse bins or flush in toilet was for the safety of children and adults at home. During the assessment, it was evident that respondents wanted to ensure safety at their homes, but failed to recognize the negative consequences to the environment by incorrect disposal practices. It has been widely reported that improper medicine disposal may lead to environmental contamination. Studies conducted in the Msunduzi and Umngeni rivers in Kwazulu-Natal, South Africa found traces of pharmaceuticals in water destined for consumption.^(71, 72)

Environmental contamination however remains unavoidable in certain instances such as medicine being excreted unchanged, or through veterinary medicine administered to livestock. Making use of drainage systems to dispose unused medicine will contribute to contamination of underground drinking water.

3.8. Adherence assessment amongst respondents

Adherence assessment was performed on all the participants. Participants had to indicate their likelihood to complete prescribed medicine by means of a 3-point Likert scale (Table 9).

Table 9. Probability to complete prescribed treatment

Response	Frequency(n)	Percentage
Uncertain	2	1.6%
Less likely	9	7.1%
Very likely	116	91.3%
Total	127	100%

Almost all the participants (91.3%) indicated that they were very likely to complete their medicine as prescribed. Only 7.1% of the respondents indicated that they would not complete medicine as prescribed and dispensed to them.

There is a large discrepancy between answers from respondents under point 3.5 on the reasons for having unused medicine, compared to the responses given under adherence assessment in point 3.8. This may be the indication that people to a great extent answer what they think is the correct way to act, rather than how they truly act. About 7.1% of the respondents stated that they were less likely to complete prescribed treatment which is not the most correct response. The observed responses of non-adherence was much higher at 36%. Hypothetical answers are usually skewed as observed in a study conducted in Sweden over a three years period (2001, 2004 and 2007), answers given kept changing every time despite the same question being asked to the same respondents.⁽⁶⁷⁾

In an effort to alleviate the strain on the healthcare system, it has been observed that certain health facilities issue three months of medication to patients who are responsive to treatment, and therefore does not require monthly follow up assessments. However, noble the intent, this practice may contribute to medicine wastage and should preferably be avoided. These practices reduce the amount of time spent with patient during dispensing of medicine and providing counselling on the correct use, storage and disposal of medicine because medicine comes readily packaged. This usually has a direct impact on the quality of pharmaceutical service rendered, leading to low adherence and medicine wastage.

3.9. Medicine return assessment

An assessment of the likelihood for patients to return expired or unused medicine back to the pharmacy was performed in a similar fashion as to measuring adherence (Table 10).

Table 10. Probability to return unused or expired medicine to pharmacy for proper disposal

Response	Frequency(n)	Percentage
Uncertain	11	8.7%
Less likely	68	53.5%
Very likely	40	31.5%
No Response	8	6.3%
Total	127	100%

Only 19.6% of the respondents in this study returned unused and expired medicine to pharmacy for safe disposal during the two weeks medicine take back or medicine return program (refer to section 3.3). When participants were asked about the likelihood to return medicine to the pharmacy; 31.5% indicated that they would do so. It was noted that more than half (53.5%) were less likely to return unused medicine (which is supported by the observation that 77% of all those who had unused or expired medicine in 2016 made use of improper disposal practices – section 3.7). When compared to 35% of the respondents who had unused or expired medicine in 2016, only 14% indicated that they returned unused or expired medicine to pharmacy for safe disposal as reported in section 3.7 above. The responses given in section 3.7 correlated with the responses under section 3.9. All those who reported that they had returned medicine to pharmacy responded to the hypothetical question that they would mostly return unused or expired medicine to pharmacy for safe disposal. The number became skewed as even those participants who never returned medicine to pharmacy but rather made use of improper disposal methods hypothetically stated that they would mostly return unused or expired medicine to pharmacy. The number became skewed by about 17.5%. It is assumed that this may be due to patients' lack of money to travel to the nearest health facility. They would rather wait to return any unused or expired medicine the same time when attending SBAH or collecting their monthly repeat prescription.

Participants were furthermore asked if they would consider returning unused or expired medicine to pharmacy for safe disposal if they had to pay for the proper disposal of their unused and expired medicine. More than three quarters (80.3%) of all the respondents indicated that they would not return unused or expired medicine for safe disposal if they were expected to contribute towards the cost involved with the destruction process of such medicine. Only 19.7% indicated that they were willing to return medicine for safe disposal if a monetary fee was enforced. South African government health facilities, including SBAH, do not enforce any collection, or additional payments for expired or unused medicine to be disposed on a patient's behalf. The destruction cost is covered by the provincial Department of Health through contracts with accredited pharmaceutical waste disposal companies.

Respondents were further asked if they were aware of the price (value) of the medicine they receive from the state. Similarly, only 15.8% pointed out that they had an estimate of the medicine value, while the majority (84.2%) were completely unaware of the financial value. The low number of people aware of pharmaceutical expenses and the tariff incurred may be explained by those patients making use of both the public and private healthcare as detailed in Table 6. As mentioned in section 3.5, patients show a general distrust in the public healthcare system, whereby they prefer obtaining their medicine from private institutions during periods when personal finances permit the additional expense. In the setting of this study population, the majority of patients are reliant on the government to take care of their healthcare needs and are therefore seldom exposed to the reality of medicine premiums.

It is of serious concern that 75.7% of the respondents who indicated that they were unaware of their medicine cost, still pointed out that they would not change the way they use medicine even if they were made aware of the financial burden on the healthcare budget. Only 24.3% recorded that it would have changed the way they use medicine at home if they comprehended the outlay of pharmaceutical expenses incurred by the government.

3.10. Importance of medicine return assessment

Patients were also assessed on the subjective importance of different apprehensions determining their reasons for completing prescribed treatment, and returning unused or expired medicine back to the pharmacy (Table 11).

Table 11. Reasons for completing treatment and returning unused medicine to pharmacy

Reason	No response (%)	Less important (%)	Important (%)	Very important (%)
Safety of children at home	10.2%	3.9%	3.2%	82.7%
Safety of adults at home	7.1%	9.4%	18.9%	64.6%
Safety of household pets	26.8%	24.4%	11.8%	37.0%
Impact of unused medicine on the environment	24.4%	29.9%	11.0%	34.7%
Cleaning medicine cabinet	12.6%	10.2%	28.4%	48.8%
Fear of using expired medicine	1.6%	2.4%	6.3%	89.8%

Most of the respondents (89.8%) reported that the fear of using expired medicine was the most likely reason they would consider to safely discard medicine or return these products to pharmacy. Only 2.4% indicated that accumulating expired medicine was not a determining factor for its safe disposal. Accumulation of excess medicine (expired or improperly stored) can present additional health risks such as poisoning, addiction or treatment failure. Correspondingly, 82.7% cited fear for the safety of their children as a motivating factor to complete treatment or dispose of any unused or expired medicine.

A meagre 3.9% did not seem to regard the safety of their children to be a determining factor for medicine disposal. Other likely reasons for safe disposal included concern for the safety of adults (64.6%), and the safety of their pets (37%). Almost half (48.8%) of the respondents documented that they essentially only dispose of unused or expired medication when cleaning their medicine cabinet, while 34.7% reported on the negative impact of unused medicine on the environment. This statement appears tilted, since it was shown that approximately 77% of expired medicine are discarded improperly by throwing in refuse bin or flush in toilet or drain; ultimately posing environment risks. As previously discussed under point 3.7. hypothetical responses don't correspond with the actual response given.

Chapter 4 – Conclusion and recommendations

The “Medicine take back or medicine return program” indicated that only a small proportion 20% (p~0.2) of patients returned unused or expired medicine to hospital pharmacy for safe disposal. SBAH pharmacy dispenses approximately 56000 medicines per month which is equivalent to 28000 medicines per two weeks. The proportion of medicine return to dispensed medicine is 34/28000 (0.12%). Many respondents were non-adherent to their treatment regimen. It was evident that most patients taking acute medicine (67%), and less of those on chronic treatment, was using their medicine as prescribed. There is a need to educate patients on the importance of adherence since most individuals seems to use medicine only when they feel it necessary to, therefore ignoring the prescribed instructions.

Most returned medicines were pharmaceutical agents used for the treatment of chronic conditions. These conditions included cardiovascular agents, antidiabetics, anti-epileptics, respiratory agents and corticosteroids. Some of the reasons contributing to these medicines being returned were attributed to medicine changes by the prescribing physician, undesirable side effects or ineffectiveness of the treatment. It is recommended that newly diagnosed patients requiring chronic treatment should be supplied with minimum quantity of medicine for a shorter period of time and with shorter intervals between consultations while being monitored more frequently until adherence is established.⁽⁹⁵⁾ Appropriate long-term treatment (six months repeatable prescription) may be considered in patients who are responsive to treatment once undesirable side effects and treatment failure has been excluded. This may increase adherence and reduce medicine change or discontinuation due to treatment failure and undesirable side effects. There is a need to look at extra financial burden put on poor patients making use of public facilities to obtain further supply of medicine or to assess the effectiveness when issued with minimum supply of medicine with multiple visits to the hospital for review and monitoring for newly diagnosed patients to prevent treatment failure.⁽⁴⁵⁾ Multidisciplinary (physicians, pharmacists and nurses) interventions taking the rational use of medicine into account may reduce medicine wastage due to non-adherence, undesirable side effects, treatment duplication or over-supply.

The cost of returned medicines to SBAH was found to be lower compared to average returns during the previous financial year. The value of returned medicine during the study period was calculated to be R652.11; however different reasons for the low response may be present. There could be different factors contributing to low turnout such as fear of being identified, high travel costs, socio-economic status and short study period. It should be noted that this medicine cost reported above does not include any medicine that was returned from the ward or expired in the pharmacy, it was medicine returned by respondents.

Most of the respondents who participated in the study improperly stored medicine at home. It was noted that the most common place to store medicine was in kitchen cupboards where these agents were exposed to high temperatures and humidity as a result of food preparation. Medicine was also found to be stored in bathroom cabinets where humidity and moisture could negatively affect the stability of these products. Medicine stored inappropriately may therefore be rendered ineffective, or lack therapeutic benefits, if degradation of the active pharmaceutical ingredients occurs. It is concluded that in general, most patients lack knowledge regarding proper storage of medicine.

Similarly, it was found that the public's knowledge on correct disposal practices were inadequate. Only 13.6% returned medicine to pharmacy for safe disposal. This study established that more than 75% of all expired or unused medicines were discarded through various unsafe methods. The disposal methods correlate well with international practices such as throwing in refuse bins, flushing down the toilet or draining in the kitchen sink. It is therefore recommended that medicine packaging should include a warning not to dispose unused or expired products in the sewerage or municipal refuse bins, but to return it to pharmacy for safe disposal. Private pharmacies should be motivated to accept unused or expired medicine from patients to motivate the public to return any unused or expired medicine. In certain circumstances government should take charge in financing destruction process of all medicine from patients.

Government should consider to increase the amount and accessibility of safe medicine drop off points such as the existing contracted CCMDDD medicine pick up points. There is a need for government to partner with private sector as improper disposal practices may result in poisoning, drug abuse or contamination of recycled water sources. Unless stricter criteria, patient awareness and education are prioritized, the current trends of inappropriate medicine disposal will continue.

Large number of patients in possession of unused or expired medicine should raise concern to the prescribers and pharmacists. Patients need to be educated on proper storage and safe disposal practices of medicine, ⁽⁹⁵⁾ It has been noted in a study conducted in Australia that respondents were willing to return unused and expired medicine once they have been made aware of the dangers in accumulating or unsafe disposal practices.⁽⁶⁰⁾ Emphasis should be placed on the importance of adhering to prescribed treatment. There is a need to re look at prescribing repeat prescription for medicine that are to be used when necessary, such as analgesics used in the management of pain .By informing health care providers on adherence related challenges and better communication between administrative personnel, prescribers and pharmacists, significant funds could be saved or redistributed, to other priority areas in the public pharmaceutical sector.

Hospital clerks tasked with making follow up appointments or medicine collection dates should do so at intervals corresponding to end of treatment date and not according to openings in the booking register. The implementation of biometric identification, electronic dispensing and record keeping should be fast-tracked in order to better equip the pharmacist to limit oversupply and monitor treatment adherence. A nationally linked biometric database may in addition prove beneficial, especially at down referral clinics to avoid the supply of incorrect medicine or inappropriate dosage strengths and to reduce the number of patients making use of multiple health facilities to collect the same treatment.

Employing designated professionals in these areas will therefore reduce medicine wastage, irrational medicine use and dispensing errors. There is an increased urgency to further explore the reasons for medicine accumulation and expiry in the South African population. The effort and process of disposing expired pharmaceuticals according to the medicine and related substance control act 101 of 1965 is a costly procedure. Making patients aware of the value of pharmaceutical services they receive, including the expensive destruction process, may lead to increased adherence and saving on pharmaceutical expenditure thereby reducing medicine wastage.

4.1. Limitations and bias

Bias was eliminated to a certain extent by the researcher being exclusively responsible for the collection of expired medicine and administration of the questionnaires, making use of face-to-face interviews in the participant's home language. A non-standardized, self-developed questionnaire was used as data collection tool, based on findings from published literature on the subject. No validation of the questionnaire was performed.

Although the population sample size was calculated to be statistically representative of the patients attending the SBAH pharmacy, the population did not comprise of individuals making use of the private healthcare system, or those attending rural government clinics. Conducting the study in a public hospital setting favored participants with a lower level of income and education. The patterns and trends of medicine wastage and disposal are only applicable to the institution where the study was managed. Despite the fact that anonymity and confidentiality was assured, and no identifiable information was recorded, many patients seemed reluctant to participate in fear of them being victimized by the healthcare professionals, or labeled as contributors to medicine wastage. The common belief was that their participation could negatively affect their future treatment and supply of medicine, thereby avoiding contact with the investigator.

The study had a low turnover of respondents returning unused or expired medicine due to the short data collection period. This may explain the seemingly decline in returned medicine compared to previous years. A similar study with a prolonged collection period and participation sites may yield different results, as patients may prefer to return unused or expired medicine at the time of collecting their monthly prescriptions or follow up consultations. There is a need to conduct similar larger studies in South Africa for a longer duration of time.

References

1. West LM. Medication wastage: the current situation. *Journal of the Malta College of Pharmacy Practice*. 2015;21:25-28.
2. Morgan TM. The economic impact of wasted prescription medication in an outpatient population of older adults. *Journal of Family Practice*. 2001;50(9):779-781.
3. Abou-Auda HS. An economic assessment of the extent of medication use and wastage among families in Saudi Arabia and Arabian Gulf countries. *Clinical therapeutics*. 2003;25(4):1276-1292.
4. Crisóstomo S, Mendes Z, Marques FB, Martins P, Rodrigues V, Ribeiro CF. Wastage of medicines in Portugal. *Value in Health*. 2006;9(6):A211.
5. Odendaal N. [internet]. Gauteng allocates large chunk of 2018/19 budget to health and education. *Creamer media's engineering news*; [updated 2018 March 06; cited 2018 November 30]. Available from: <http://www.engineeringnews.co.za/article/gauteng-allocates-large-chunk-of-201819-budget-to-health-education-2018-03-06>.
6. Mahlangu Q. [internet] 2015/16 health budget vote speech tabled by the MEC for Health Ms Qedani Mahlangu at the Gauteng Legislature on 19 June 2015 [updated 2015 June 19; cited 2018 November 30]. Available from: https://serve.mg.co.za/content/documents/2017/10/23/qwruow0uTf2SNrdw8DIm_Gauteng_department_of_health_2015_budget_speech_tabled_by_Qedani_Mahlangu.pdf.
7. Naidoo S. The South African national health insurance: A revolution in health-care delivery! *Journal of Public Health*. 2012;34(1):149-150.
8. Vellinga A, Cormican S, Driscoll J, Furey M, O'Sullivan M, Cormican M. Public practice regarding disposal of unused medicines in Ireland. *Science of the Total Environment*. 2014;478:98-102.
9. Al-Siyabi K, Al-Riyami K. Value and types of medicines returned by patients to Sultan Qaboos University Hospital pharmacy, Oman. *Sultan Qaboos University Medical Journal*. 2007;7(2):109.
10. Braund R, Gn G, Matthews R. Investigating unused medications in New Zealand. *Pharmacy world & science*. 2009;31(6):664.
11. Abahussain EA, Ball DE, Matowe WC. Practice and opinion towards disposal of unused medication in Kuwait. *Medical Principles and Practice*. 2006;15(5):352-357.

12. Ekedahl AB. Reasons why medicines are returned to Swedish pharmacies unused. *Pharmacy World and Science*. 2006;28(6):352-358.
13. James TH, Helms ML, Braund R. Analysis of medications returned to community pharmacies. *The Annals of Pharmacotherapy*. 2009;43(10):1631-1635.
14. Auta A, Omale S, Shalkur D, Abiodun AH. Unused medicines in Nigerian households: Types and disposal practices. *Journal of pharmacology & pharmacotherapeutics*. 2011;2(3):195.
15. Braund R, Peake BM, Shieffelbien L. Disposal practices for unused medications in New Zealand. *Environment International*. 2009;35(6):952-955.
16. Tong A, Peake B, Braund R. Disposal practices for unused medications in New Zealand community pharmacies. *Journal of primary health care*. 2011;3(3):197-203.
17. Vollmer G. Disposal of pharmaceutical waste in households—a European survey. *Green and Sustainable pharmacy: Springer*; 2010.165-178.
18. Tong AY, Peake BM, Braund R. Disposal practices for unused medications around the world. *Environment international*. 2011;37(1):292-298.
19. The Constitution of the Republic of South Africa, Pub. L. No. Act No 5 of 2005 Stat. Act, 108 of 1996 (4 February 1997, 1996).
20. Lehohla P. Use of health facilities and levels of selected health conditions in South Africa: Findings from the General Household Survey, 2011. Pretoria: Statistics South Africa. 2011;report no03-00-05:7-23.
21. Herman P. [internet]. 81% of households that use public healthcare 'satisfied' - Stats SA.News24; [updated 2018 June 22; Cited 2018 December 05] Available from: <https://www.news24.com/SouthAfrica/News/81-of-households-that-use-public-healthcare-satisfied-stats-sa-20180622>.
22. Gordhan P. Budget speech. Pretoria: Communications Unit, National Treasury. 2016;report no 17.
23. Kettledas R. [internet]. central chronic medicine dispensing and distribution programme. National department of health; [updated 2016 June 19; cited 2018 June 15]. Available from: https://za.usembassy.gov/wp-content/uploads/sites/19/2016/06/Central-Chronic-Medicine-Dispensing-and-Distribution-Programme_Ricardo-Kettledas.pdf.

24. Health-eNewsreport. Health-e News report [internet]. SA's new medicines dispensing programme a 'major benefit'. Medical brief Africa's medical media digest; [updated 2018 January 31; cited 2018 December 02]. Available from: <https://www.medicalbrief.co.za/archives/sas-new-medicines-dispensing-programme-major-benefit/>.
25. Nash D. South Africa's Medicines and Related Substances Control Amendment Act of 1997. Berkeley Technology Law Journal. 2000;485-502.
26. Thomas L. Tonnes of medicine wastage costs millions. Australian nursing & midwifery journal. 2015;23(1):24.
27. West LM, Theuma RB, Cordina M. Determination of medicines wastage and its association with beliefs about medicines and locus of control in patients suffering from chronic conditions—A pilot study. Research in Social and Administrative Pharmacy. 2017;13(3):e6-e7.
28. Organization WH. The pursuit of responsible use of medicines: sharing and learning from country experiences. 2012;WHO/Emp/Mar/2012:3.
29. Ewen S, Baumgarten T, Rettig-Ewen V, Mahfoud F, Griese-Mammen N, Schulz M, et al. Analyses of drugs stored at home by elderly patients with chronic heart failure. Clinical Research in Cardiology. 2015;104(4):320-327.
30. Hoffman JM, Shah ND, Vermeulen LC, Hunkler RJ, Hontz KM. Projecting future drug expenditures--2004. American Journal of Health-System Pharmacy. 2004;61(2):145-158.
31. White KG. UK interventions to control medicines wastage: a critical review. International Journal of Pharmacy Practice. 2010;18(3):131-140.
32. Wilson PM, Kataria N, McNeilly E. Patient and carer experience of obtaining regular prescribed medication for chronic disease in the English National Health Service: a qualitative study. BMC health services research. 2013;13(1):192.
33. Taylor D. Reducing medicines wastage through improving patient care. Prescriber. 2011;22(7):5-7.
34. Hassali MA, Supian A, Ibrahim MI, Al-Qazaz HK, Al-Haddad M, Saleem F, et al. The Characteristics of Drug Wastage at the Hospital, Tuanku Jaafar Seremban, Malaysia: A Descriptive Study. Journal of Clinical & Diagnostic Research. 2012;6(5):787-790.
35. Law AV, Sakharkar P, Zargarzadeh A, Tai BWB, Hess K, Hata M, et al. Taking stock of medication wastage: unused medications in US households. Research in Social and Administrative Pharmacy. 2015;11(4):571-578.

36. Maeng DD, Snyder RC, Medico CJ, Mold WM, Maneval JE. Unused medications and disposal patterns at home: Findings from a Medicare patient survey and claims data. *Journal of the American Pharmacists Association*. 2016;56(1):41-46.
37. Kusturica MP, Tomic Z, Bukumiric Z, Horvat O, Pavlovic N, Mikov M, et al. Antibiotics in Serbian Households: a Source of Potential Health and Environmental Threats? *Central European journal of public health*. 2015;23(2):114.
38. Khader N, Lashier A, Yoon SW. Pharmacy robotic dispensing and planogram analysis using association rule mining with prescription data. *Expert Systems with Applications*. 2016;57:296-310.
39. Nemutanzhela P, Sekgweleo, T. Robotic technology for optimizing dispensing chronic medication in South Africa Healthcare centers. *International journal of sciences: Basic and applied research*. 2014;18(2):61-67.
40. Right to care. [internet]. Pharmacy automation. Right to care; [cited 2018 December 05]. Available from: <http://righttocare.org/innovations/pharmacy-automation/>.
41. Ruhoy IS, Daughton CG. Beyond the medicine cabinet: An analysis of where and why medications accumulate. *Environment international*. 2008;34(8):1157-1169.
42. Gracia-Vásquez SL, Ramírez-Lara E, Camacho-Mora IA, Cantú-Cárdenas LG, Gracia-Vásquez YA, Esquivel-Ferriño PC, et al. An analysis of unused and expired medications in Mexican households. *International journal of clinical pharmacy*. 2015;37(1):121-126.
43. Daukšienė J, Radžiūnas R. Nonadherence to medications among pharmacy clients and their attitude toward medications kept a medicine cabinet at home. *Medicina*. 2009;45(12):1013-1018.
44. Chien H-Y, Ko J-J, Chen Y-C, Weng S-H, Yang W-C, Chang Y-C, et al. Study of medication waste in Taiwan. *Journal of Experimental & Clinical Medicine*. 2013;5(2):69-72.
45. West LM, Diack L, Cordina M, Stewart D. A systematic review of the literature on 'medication wastage': an exploration of causative factors and effect of interventions. *International journal of clinical pharmacy*. 2014;36(5):873-881.
46. Lystlund S, Stevens E, Planas LG, Marcy TR. Patient participation in a clinic-based community pharmacy medication take-back program. *Journal of the American Pharmacists Association*. 2014;54(3):280-284.

47. Azad M, Kalam A, Ansary M, Haque R, Akhter M, Al-Mamun S, et al. Disposal Practice for Unused Medications among the Students of the International Islamic University Malaysia. 2012;2(7):101-106.
48. Kagashe GA, Makenya FB, Buma D. Medicines Wastage at a Tertiary Hospital in Dar Es Salaam Tanzania. *Journal of Applied Pharmaceutical Science*. 2014;4(6):98-102.
49. Ellis JC, Mullan J, Worsley T. Prescription medication hoarding and borrowing or sharing behaviours in older residents in the Illawarra, New South Wales, Australia. *Australasian journal on ageing*. 2011;30(3):119-123.
50. Bekker CL, Gardarsdottir H, Egberts TC, Bouvy ML, van den Bemt BJ. Redispensing of medicines unused by patients: a qualitative study among stakeholders. *International journal of clinical pharmacy*. 2017;39(1):196-204.
51. Gilmartin JFM, Jani Y, Smith F. Exploring the past, present and future of care home medicine management systems: pharmacists' perceptions of multicompartment compliance aids. *J Pharm Health Serv Res*. 2015;6(4):177-184.
52. Mackridge AJ, Marriott JF. Returned medicines: waste or a wasted opportunity? *Journal of Public Health*. 2007;29(3):258-262.
53. Council SAP. *Good pharmacy practice in South Africa*: Government Printer, South Africa; 2004.
54. Kozak MA, Melton JR, Gernant SA, Snyder ME. A needs assessment of unused and expired medication disposal practices: A study from the Medication Safety Research Network of Indiana. *Research in Social and Administrative Pharmacy*. 2016;12(2):336-340.
55. Frontières MS, Frontières PS. Guidelines for safe disposal of unwanted pharmaceuticals in and after emergencies. *World Health Organization*. 1999:11-17.
56. McClinton M. Safe destruction of medicine and medical devices (A-thermal retort technologies). Workshop-Good wholesale distribution practices for medical products and medical dVICES; 2018 August 14-16; Midrand ;South Africa.
57. Renckens S. The Basel Convention, US politics, and the emergence of non-state e-waste recycling certification. *Int Environ Agreem-Polit Law Econom*. 2015;15(2):141-158.

58. Raphela S. Treatment and disposal of medical waste in rural and urban clinics within Polokwane municipality of South Africa. *Journal for New Generation Sciences*. 2014;12(2):97-109.
59. Gabela SD, Knight SE. Healthcare waste management in clinics in a rural health district in KwaZulu-Natal. *Southern African Journal of Epidemiology and Infection*. 2010;25(1):19-21.
60. Bettington E, Spinks J, Kelly F, Gallardo-Godoy A, Nghiem S, Wheeler AJ. When is a medicine unwanted, how is it disposed, and how might safe disposal be promoted? Insights from the Australian population. *Australian Health Review*. 2017;42(6):709-717.
61. Arkaravichien W, Ruchipiyarak T, Thawinwan W, Benjawilaikul S. A Threat to the Environment from Practice of Drug Disposal in Thailand. *EnvironmentAsia*. 2014;7(1):13-18.
62. Glassmeyer ST, Hinchey EK, Boehme SE, Daughton CG, Ruhoy IS, Conerly O, et al. Disposal practices for unwanted residential medications in the United States. *Environment international*. 2009;35(3):566-572.
63. Sasu S, Kümmerer K, Kranert M. Assessment of pharmaceutical waste management at selected hospitals and homes in Ghana. *Waste Management & Research*. 2012;30(6):625-630.
64. Bashaar M, Thawani V, Hassali MA, Saleem F. Disposal practices of unused and expired pharmaceuticals among general public in Kabul. *BMC Public Health*. 2017;17(1):45.
65. Maharana SP, Paul B, Dasgupta A, Garg S. Storage, reuse, and disposal of unused medications: A cross-sectional study among rural households of Singur, West Bengal. *International journal of medical science and public health*. 2017;6(7):1185-1189.
66. El-Hamamsy M. Unused Medications: how cost and how disposal of in Cairo, Egypt. *International Journal of Pharmaceutical studies and research*. 2011;2(1):21-27.
67. Persson M, Sabelström E, Gunnarsson B. Handling of unused prescription drugs—knowledge, behaviour and attitude among Swedish people. *Environment international*. 2009;35(5):771-774.
68. Murdoch K. Pharmaceutical Pollution in the Environment: Issues for Australia, New Zealand and Pacific Island countries. *National toxic network*. 2015.

69. Bruce GM, Pleus RC, Snyder SA. Toxicological relevance of pharmaceuticals in drinking water. *Environmental science & technology*. 2010;44(14):5619-5626.
70. Parwana H. Pharmaceuticals in Drinking Water?. *Science reporter*. 2012:30-31.
71. Agunbiade FO, Moodley B. Pharmaceuticals as emerging organic contaminants in Umgeni River water system, KwaZulu-Natal, South Africa. *Environmental monitoring and assessment*. 2014;186(11):7273-7291.
72. Agunbiade FO, Moodley B. Occurrence and distribution pattern of acidic pharmaceuticals in surface water, wastewater, and sediment of the Msunduzi River, Kwazulu-Natal, South Africa. *Environmental toxicology and chemistry*. 2016;35(1):36-46.
73. Roig B, D'Aco V. Distribution of pharmaceutical residues in the environment. *Issues in Environmental Science and Technology*. 2015:34-69.
74. Organization WH. Pharmaceuticals in drinking-water. 2012;WHO/HSE/WSH/11.05:1-6.
75. Nutt D, King LA, Saulsbury W, Blakemore C. Development of a rational scale to assess the harm of drugs of potential misuse. *The Lancet*. 2007;369(9566):1047-1053.
76. Kümmerer K. Pharmaceuticals in the environment. *Annual review of environment and resources*. 2010;35:57-75.
77. Bull RJ, Crook J, Whittaker M, Cotruvo JA. Therapeutic dose as the point of departure in assessing potential health hazards from drugs in drinking water and recycled municipal wastewater. *Regulatory Toxicology and Pharmacology*. 2011;60(1):1-19.
78. Jones OA, Lester JN, Voulvoulis N. Pharmaceuticals: a threat to drinking water? *Trends in Biotechnology*. 2005;23(4):163-167.
79. Grelotti DJ, Closson EF, Smit JA, Mabude Z, Matthews LT, Safren SA, et al. Whoonga: Potential Recreational Use of HIV Antiretroviral Medication in South Africa. *AIDS Behav*. 2014;18(3):511-518.
80. Berckmans P, Dawans V, Schmets G, Vandenberghe D, Autier P. Inappropriate drug-donation practices in Bosnia and Herzegovina, 1992 to 1996. *New England journal of medicine*. 1997;337:1842-1845.

81. Sonowal S, Desai C, Kapadia JD, Desai MK. A Survey of Knowledge, Attitude, and Practice of Consumers at a Tertiary Care Hospital Regarding the Disposal of Unused Medicines. *Journal of basic and clinical pharmacy*. 2016;8(1):4.
82. Veale DJH, Wium CA, Müller GJ. Toxicovigilance I: A survey of acute poisonings in South Africa based on Tygerberg Poison Information Centre data. *SAMJ: South African Medical Journal*. 2013;103(5):293-297.
83. Vaughn LM, Donohoe K. Dangers in the medicine cabinet appropriate management of expired and unused prescription drugs. *Home Health Care Management & Practice*. 2013;25(4):155-159.
84. Peden M, Unicef, World Health O. World report on child injury prevention. 2008.
85. Langley C, Marriott J, Mackridge A, Daniszewski R. An analysis of returned medicines in primary care. *Pharmacy World and Science*. 2005;27(4):296-299.
86. Asti L, Jones R, Bridge JA. Acetaminophen and expired medication storage in homes with young children. *Journal of Clinical Toxicology*. 2013;2012.
87. Malangu N, Ogunbanjo G. A profile of acute poisoning at selected hospitals in South Africa. *Southern African Journal of Epidemiology and Infection*. 2009;24(2):14-16.
88. Kasule M, Malangu N. Profile of acute poisoning in three health districts of Botswana. *African Journal of Primary Health Care and Family Medicine*. 2009;1(1):22-27.
89. Najafi F, Beiki O, Ahmadijoubary T, Amini S, Moradinazar M, Hatemi M, et al. An assessment of suicide attempts by self-poisoning in the west of Iran. *Journal of forensic and legal medicine*. 2014;27:1-5.
90. Bicket MC, Long JJ, Pronovost PJ, Alexander GC, Wu CL. Prescription opioid analgesics commonly unused after surgery: a systematic review. *JAMA surgery*. 2017;152(11):1066-1071.
91. Absoul-Younes A, Wazaify M, Yousef AM, Tahaineh L. Abuse and misuse of prescription and nonprescription drugs sold in community pharmacies in Jordan. *Substance use & misuse*. 2010;45(9):1319-1329.
92. Al-Wazaify M, Absoul-Younes A. Pharmacy in Jordan. *American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists*. 2005;62(23):2548-2551.

93. Bettington E, Spinks J, Kelly F, Wheeler AJ. Returning unwanted medicines to pharmacies: prescribing to reduce waste. Australian Prescriber. 2018;41(3):78.
94. Healthman. [internet]. NHI white paper 2017 summary. Healthman ; [cited 2018 December 12].Available from:
<https://www.mm3admin.co.za/documents/docmanager/1E9AEA2C-B58D-4AED-B5A2-96187D705AEE/00126403.pdf>.
95. Bergen PJ, Hussainy SY, George J, Kong DC, Kirkpatrick CM. Safe disposal of prescribed medicines. Australian prescriber. 2015;38(3):90.

Appendices

Appendix 1: Patient information and informed consent document (PICD2)

PATIENT OR PARTICIPANT'S INFORMATION & INFORMED CONSENT DOCUMENT

STUDY TITLE: Proportional determination and reasons for medication returns at a tertiary academic hospital in Gauteng

SPONSOR: Department of Research and Innovation support, university of Pretoria

Principal Investigators: Maluleke Enos Eric

Institution: University of Pretoria

DAYTIME AND AFTER-HOURS TELEPHONE NUMBER(S):

Daytime numbers: 0113866060

Afterhours: 0833737748

DATE AND TIME OF FIRST INFORMED CONSENT DISCUSSION:

Day	Month	Year

:
Time

Dear Patient

Dear Mr. / Mrs. date of consent procedure/...../.....

1) INTRODUCTION

You are hereby invited to volunteer to participate in a research study. This information leaflet is to help you to decide if you would like to participate. Before you agree to take part in this study you should fully understand what is involved. If you have any questions, which are not fully explained in this leaflet, do not hesitate to ask the investigator. You should not agree to take part unless you are completely happy about all the procedures involved. In the best interests of your health, it is strongly

recommended that you discuss with or inform your personal doctor of your possible participation in this study, wherever possible.

2) THE NATURE AND PURPOSE OF THIS STUDY

You are invited to take part in a research study. The aim of this study is to determine the proportion and reason for medication return at a tertiary academic hospital in Gauteng. The aim of this study is to find out what the possible reasons are for having excess and expired medicine at homes and the methods used to dispose of the medications. By knowing this we would be able to better communicate and educate the dangers of medicine accumulation and improper disposal practices to the community, and prevent medication wastage

3) EXPLANATION OF PROCEDURES TO BE FOLLOWED

The questionnaire will be administered telephonically or in person by principal investigator according to the answers you provide. It will not take more than 10 minutes of your time. Although your information will be available to me, you will not be identified in any collection of data and processing of the data will therefore be anonymous and confidential. You will not be penalized for your honest answers and this will not impact any future treatment you may receive from Steve Biko Academic Hospital or medicines you receive from the pharmacy.

4) RISK AND DISCOMFORT INVOLVED.

There is no possible risk and discomfort involved in participating in the study. The study is only questionnaire.

5) POSSIBLE BENEFITS OF THIS STUDY.

There will be no direct benefit to you, but your participation would enable us to find out more on how to prevent medicine wastage, poisoning, and environmental impact due to improper disposal of medication. It will also enable the hospital to adjust and better allocate the strict budget they receive from the provincial government for pharmaceuticals. You will not receive any financial incentive or refund for returning unused medication or participating in the study. If needed, we will assist you with traveling expenses for purposes relating to this project only

6) I understand that if I do not want to participate in this study, I will still receive Pharmaceutical service at the hospital.

7) I may at any time withdraw from this study.

8) HAS THE STUDY RECEIVED ETHICAL APPROVAL?

This Protocol has been approved by the Faculty of Health Sciences Research Ethics Committee, University of Pretoria, telephone numbers 012 356 3084 / 012 356 3085. The study has been structured in accordance with the Declaration of Helsinki (last update: October 2013), which deals with the recommendations guiding students in biomedical research involving human/subjects. A copy of the Declaration may be obtained from the investigator should you wish to review it.

9) INFORMATION If I have any questions concerning this study, I should contact:

Mr Maluleke Enos Work tel :011386 6060 or cell: 0833737748

10) CONFIDENTIALITY

All records obtained whilst in this study will be regarded as confidential. Results will be published or presented in such a fashion that patients remain unidentifiable.

11) CONSENT TO PARTICIPATE IN THIS STUDY.

I have read or had read to me in a language that I understand the above information before signing this consent form. The content and meaning of this information have been explained to me. I have been given opportunity to ask questions and am satisfied that they have been answered satisfactorily. I understand that if I do not participate it will not alter my management in any way. I hereby volunteer to take part in this study.

I have received a signed copy of this informed consent agreement.

.....
Patient name	Date
.....
Patient signature	Date
.....
Investigator's name	Date
.....
Investigator's signature	Date
.....
Witness name and signature	Date

VERBAL PATIENT INFORMED CONSENT

I, the undersigned, Mr, have read and have explained fully to the patient, named and/or his/her relative, the patient information leaflet, which has indicated the nature and purpose of the study in which I have asked the patient to participate. The patient indicated that he/she understands that he/she will be free to withdraw from the study at any time for any reason and without jeopardizing his/her treatment.

I hereby certify that the patient has agreed to participate in this study.

Patient's Name _____
(Please print)

Patient's Signature _____ Date _____

Investigator's Name _____
(Please print)

Investigator's Signature _____ Date _____

Witness's Name _____ Witness's Signature _____ Date _____
(Please print)

Appendix 2: Questionnaire

Identification		Age Group		Gender			Race			
Patient		18-20		Male	Female	Other	Black	white	Colored	Other
Care giver		21-30	61-70							
Family		31-40	71-80							
Date		41-50	81-90							
		51-60	91-100							
1.	Are you currently taking any medication to manage pain?								Yes	No
1.1	If Yes, please specify									
1.2	Are you likely to complete the given pain medication?								Yes	No
1.3	Indicate reasons for not completing									
2.	Are you currently taking any antibiotics?								Yes	No
2.1	If yes, please mention product and condition									
2.2	Are you likely to complete the given antibiotics?								Yes	No
2.3	Indicate the reason for not completing									
3	Are you taking medicine for the following chronic diseases:(specify drug name)									
3.1	Hypertension								Yes	No
3.2	Diabetes								Yes	No
3.3	Asthma								Yes	No
3.4	Tuberculosis								Yes	No
3.5	HIV/AIDS								Yes	No
3.6	Depression or anxiety								Yes	No
3.7	Heart failure								Yes	No
3.8	Kidney failure								Yes	No
3.9	Cancer								Yes	No
3.10	Other								Yes	No
4	Do you currently have unused or expired medicine at home?								Yes	No
4.1	If yes, please mention products and quantities									
4.2	Where in your home do you keep the medicine?									
4.3	What is the reason you keep unused medicine at home?									
5	What is the reason for not completing medicine as prescribed?									

6	Did you have unused or expired medicine at home in the past year?	Yes	No		
7	How did you discard the excess medicine at home? (<i>unused and expired</i>)				
8	What was the reason for choosing that method of removing medicine from your home?				
9	Have you ever had an incident of poisoning at home?	Yes	No		
10	If yes was it intentional or accidental?				
11	How old was the person who was exposed to poisoning?				
12	Has this incident changed the way you handle, store and discard medicine at home?	Yes	No		
13	How likely are you to throw away medicine in a bin or flush in the toilet?	No Response	Less likely	Most likely	Don't know
14	How likely are you to complete the medicine as prescribed to you?	No Response	Less likely	Most likely	Don't know
15	How likely will you return unused and expired medicine to hospital pharmacy for disposal?	No Response	Less likely	Most likely	Don't know
16	How often do you collect medicine from pharmacy?				
17	How often do you use medicine?				
18	Would you return unused or expired medicine if you had to pay for the process of destruction?	Yes	No		
19	Do you know the cost of the medicine prescribed and dispensed to you?	Yes	No		
20	If No, would it have changed the way you take your medicine if you knew how much it cost government?	Yes	No		
21	How important are each of the following in your choice to consider completing prescribed medicine and returning unused and expired medicine back to pharmacy	No Response	Less important	Important	Very important
21.1	Safety of children at home and accidental and intentional exposure				
21.2	Safety of adults at home and accidental, intentional exposure or abuse of unused and expired medicine.				
21.3	Safety of household pets				
21.4	The impact of unused and expired medicine has on the environment				
21.5	Cleaning out the medicine cabinet				
21.6	Fear of using expired medicine unaware				

Appendix 3: Biostatistician letter

Date: 18 / 6 / 2018

LETTER OF CLEARANCE FROM THE BIOSTATISTICIAN

This letter is to confirm that the student(s),

with the Name(s) MR ENOS E MALULEKE

Studying at the University of PRETORIA

discussed the Project with the title Proportional determination and bearing for medication returns at a Tertiary academic hospital in Gauteng

_____ with me.

I hereby confirm that I am aware of the project and also undertake to assist with the Statistical analysis of the data generated from the project.

The analytical tool that will be used ~~will be~~ in this amended study are descriptive statistics like proportions along with 95% c.i.s and data summary re proper/improper disposal practices to achieve the objective(s) of the study.

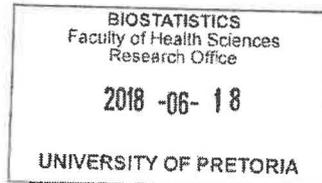
Name: PJ Becker

Date 18/6/18

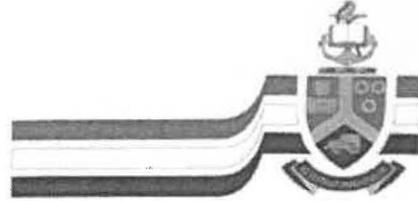
Signature _____

Tel: 012-319-2203

Research Office, Faculty of Health Sciences, University of Pretoria



Appendix 5: MMed committee approval



University of Pretoria
Faculty of Health Sciences

Department Internal Medicine
Kalafong Hospital
Klinikala Building 2-1
Tel 27-12-373 1075
e-mail: danie.vanzyl@up.ac.za

LETTER OF MMED COMMITTEE APPROVAL

This letter is to confirm that the protocol of student, **Dr Enos Maluleke**, titled "**Proportional determination and reasons for medication returns at a tertiary academic hospital in Gauteng**" has served at the MMed Committee and was found to be academically acceptable.

A handwritten signature in black ink, appearing to read 'Danie van Zyl'.

Prof DG van Zyl
Chairman: MMed Protocol Committee

Date: July 10, 2018

Please Note that you may now apply to the Ethics Committee for approval.
See http://www.up.ac.za/academic/healthsciences_old/ethics/ for requirements.

APPENDIX 6: Summary

SUMMARY

Proportional determination and reasons for medication returns at a tertiary academic hospital in Gauteng

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Summary

South Africa has a quadruple burden of disease which leads to increased pharmaceutical expenditure on communicable and non-communicable diseases. This study aimed to determine the proportion of patients that return unused or expired medicine to a tertiary academic hospital pharmacy in Gauteng, including the reasons for unused or expired medicine being returned. In addition the monetary value of the returned medication was calculated. Furthermore, common medicine disposal practices were assessed.

Data was collected by administering questionnaires to patients presenting at the Steve Biko Academic Hospital pharmacy awaiting prescription refills, or those attending for the purpose of returning unused medications.

It was found that the proportion of patients returning unused or expired medicine was approximately 20% (P=0.2). Cited reasons for accumulating expired medicine included non adherence (36%), doctor discontinued treatment (16%), undesirable side effects (12%), death (8%), oversupply (12%), incorrect medicine supplied (4%), short expiry of compounded medicine (4%), unknown reasons (4%), duplication from public and private (4%). The monetary value of all returned medicine during the two-week collection period (6 – 17 March 2017) was determined to be R652.11. This value may seem low, but did not include expired or returned medication from hospital wards, where the usage are different compared to an out-patient setting.

Cardiovascular (11.8%), anti-diabetic (11.8), corticosteroid (11.8) and respiratory agents (11.8) were among the leading medicine class returned. During the previous year (2016), more than a quarter (34.7%) of patients was in possession of unused and expired medicine, of which only (13.6%) of those returned it to the pharmacy for safe disposal. Other disposal practices consisted of flushing down the toilet/ in drain (43.2%), discarding in refuse bins (34.1%), throwing it into pit-toilets or burying in a hole (6.8%), and storing it for future use (2.3%).

It was evident from this study that only a small proportion of patients returned unused or expired medicine to pharmacy for safe disposal. The principle reasons for medicine accumulation indicate non-adherence and treatment discontinuation. This study elucidated to the fact that there is a need to educate the public on the importance of proper storage, safe disposal practices, and adherence to prescribed treatment. To increase locations where unused or expired medicines may be dropped off for safe disposal.

Keywords: Disposal practices, returned medicine, medicine wastage, non-adherence, expired medication

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