

Analysis of patient drug usage trends in the POYC scheme

*Submitted in partial fulfilment
of the requirements of the
Degree of Master of Pharmacy*

John Bryan Ruba

Department of Pharmacy
2020



L-Università
ta' Malta

University of Malta Library – Electronic Thesis & Dissertations (ETD) Repository

The copyright of this thesis/dissertation belongs to the author. The author's rights in respect of this work are as defined by the Copyright Act (Chapter 415) of the Laws of Malta or as modified by any successive legislation.

Users may access this full-text thesis/dissertation and can make use of the information contained in accordance with the Copyright Act provided that the author must be properly acknowledged. Further distribution or reproduction in any format is prohibited without the prior permission of the copyright holder.

Abstract

The Pharmacy of your Choice (POYC) scheme is part of the national health service in Malta. This pharmaceutical service provides free medicines and pharmaceutical devices for chronic diseases through private community pharmacies. The aim of this study was to analyse drug usage data within the POYC system using a community pharmacy in Malta as an example. POYC patients who are registered with the pharmacy were selected randomly using an online random number generator. Patient details and drug usage history were recorded by accessing the POYC data from a centralized computer system. Drugs were categorized into their respective therapeutic class based on the outpatients formulary list from the Ministry of Health. Drug usage data was obtained for 200 patients (107 female, 93 male, mean age 66 years (13 to 89 years)). Central nervous and cardiovascular system were the classes with the most number of drugs used. The 10 most commonly used drugs among POYC patients are simvastatin (74), amlodipine (62), aspirin (56), perindopril (56), valsartan (53), metformin (43), omeprazole (43), atorvastatin (34), bendroflumethiazide (32), and salbutamol (30). There has been an increase in the usage for 8 out of 10 drugs. The greatest rise observed was of atorvastatin, with 2,856 tablets dispensed in 2019 from 1232 dispensed tablets in 2017, a 131.8% increase. Omeprazole and salbutamol have a 26.5% and 21.6% increase, respectively. The quantity dispensed for simvastatin decreased from 4,956 in 2017 to 4,564 tablets in 2019. Dispensing of aspirin has been steady with 1976 for each year over the past 3 years. From total number of potential drug interactions, the combination of amlodipine and simvastatin was the highest in number. The study captures perspective trends of drug usage within the national health service.

Acknowledgement

I would like to express my deepest gratitude to my supervisor Professor Anthony Serracino-Inglott for providing me valuable inputs and meaningful guidance and for sharing his wisdom.

I am very much grateful to my co-supervisor Dr. Louise Grech for her meaningful assistance, tireless guidance and patience. The completion of this undertaking could not have been possible without her help.

A big thank you to my family in the Philippines and here in Malta for the constant support and for making things bearable especially during this pandemic.

Table of Contents

Abstract	ii
Acknowledgement Page	iii
Table of Contents	iv
List of Tables	vii
List of Figures	ix
List of Appendices	x
List of Abbreviations	xi
Chapter 1	
1.1. European drug usage	1
1.2. The Maltese healthcare system	1
1.3. Pharmacy of Your Choice (POYC) Scheme	3
1.3.1. Schedule V entitlement	3
1.3.2. Schedule II entitlement	4
1.3.3. Government Formulary List (GFL)	5
1.3.4. Registering within the POYC Scheme	6

1.4.	Rationale of the study	7
1.5.	Aim	7
1.5.1.	Objectives	7
Chapter 2 Methodology		8
2.1	Study Design	9
2.2	Study Setting	9
2.3	Ethical Considerations	9
2.4	Data Collection and Procedure	10
2.4.1	Patient Selection	10
2.4.2	Data Collection	10
2.4.2.1	Data Sheet	11
2.4.2.2	Demographics and History	11
2.5	Classification of medications	12
2.6	Identification of Potential Interaction of Drug Combinations	13
Chapter 3 Results		15
3.1	Demographics of the Sample	16
3.2	Number of Drugs Used According to Demographics	17
3.3	Most Common Classes of Drugs Used	17

3.4 Drugs and Their Distribution by Classification	18
3.5 Trend of 10 Most Commonly Used Drugs Across a 3-year Period	27
3.6 Drug Combinations with Potential Interactions	28
Chapter 4 Discussion	30
4.1 Demographics	31
4.2 Number of Drugs Used According to Demographics	31
4.3 Most Common Classes of Drugs Used	32
4.4 Trends of Most Commonly Used Drugs Across a 3-year Period	33
4.5 Drug Combinations with Potential Interactions	34
4.6 Potential Roles of Pharmacists	36
4.7 Limitations of the Study	37
4.8 Further Research	37
4.9 Conclusion	38
References	39
List of Publications and Abstracts	43
Appendices	44

List of Tables

Table 2.1 Classification of Medications based on GFL	12
Table 2.2 Lexicomp® Categories of Drug-Drug Interactions	14
Table 3.1 Number of Drugs Used According to Gender and Age	17
Table 3.2 Frequency of Central Nervous System Drugs Use	19
Table 3.3 Frequency of Cardiovascular System Drugs Use	20
Table 3.4 Frequency of Endocrine System Drugs Use	21
Table 3.5 Frequency of Respiratory System Drugs Use	22
Table 3.6 Frequency of Gastrointestinal System Drugs Use	23
Table 3.7 Frequency of Drugs for Eye Disorders Use	23
Table 3.8 Frequency of Drugs for Nutrition and Blood Use	24
Table 3.9 Frequency of Drugs for Skin Disorders Use	25
Table 3.10 Frequency of Drugs for Musculoskeletal and Joint Diseases Use	25
Table 3.11 Frequency of Drugs for Immunosuppression and Malignant Disease Use	26
Table 3.12 Frequency of Drugs for Infections Use	26
Table 3.13 Frequency of Drugs for Other Disorders Use	27
Table 3.14 Trend of 10 Most Commonly Used Drugs Across a 3-year Period	28
Table 3.15 Potential Interactions: frequency and risk category	29

List of Figures

Figure 2.1 Data Sheet Header	11
Figure 2.2 Dispensing History Header	12
Figure 3.1 Patient Demographics: Age	16
Figure 3.2 Most Common Classes of Drugs Used	18

List of Appendices

Appendix 1. The Schedule V Chronic Conditions	45
Appendix 2. Ethics Approval: Correspondence from FREC	47
Appendix 3. FIP Abstract	48

List of Abbreviations

AHA – American Heart Association

ATC – Anatomical Therapeutic Chemical

CNS – Central Nervous System

GDP – Gross Domestic Product

GFL – Government Formulary List

INN – International Non-proprietary Name

MAS – Medicines Approval Section

MP – Medicine Protocol

POYC – Pharmacy of Your Choice

WHO – World Health Organization

Chapter 1

Introduction

1.1. European drug usage

There is diversity of health care system models around the globe. These may vary depending on their utilisation of health costs, funding, governance, human resource, inaccessibility, and infrastructure, which will affect the delivery of health services to the community (Amber and Feroz, 2017).

The World Health Organization (WHO) 2019 global report on health spending¹ stated that from 2016-2017, there was a rapid growth in domestic spending on a global scale from and between a 17-year period (2000-2017), the global health spending increased by 3.9% a year. In the 2018 Europe Health Report,² the total retail pharmaceutical expenses of the European Union (EU) was reported to be above EUR 210 million in 2016 and also indicated a rise by 5% from 2010. On a per capita basis, Germany spent the most with around 40% above the EU average (EUR 572), followed by Ireland (EUR 498) and Belgium (EUR 491). Denmark, Romania, Estonia and Poland were among those who had the least medicine-related disbursements.

1.2. The Maltese healthcare system

In Malta, the healthcare system consists of a private sector where the patients pay for hospital and clinic visits to private clinics or hospitals and the public sector. The public sector, falls under the remit of the Government who is responsible for both the regulation and provision of health services which includes Government hospitals, clinics and

¹ Global spending on health: a world in transition. Geneva: World Health Organization; 2019 (cited 2020 Aug 11)

² OECD/EU, Health at a Glance: Europe 2018: State of Health in the EU Cycle, OECD Publishing, Paris 2018 (cited 2020 Aug 11). Available from: https://doi.org/10.1787/health_glance_eur-2018-en

residential homes. Primary and secondary care, including pharmaceuticals, and which are provided through the Government scheme are free of charge to entitled Maltese residents.

According to the WHO Global Health Expenditure Database³, the total health expenditure in Malta, reported as a percentage of Gross Domestic Product (GDP) was 9.34% in 2017 and remained at about the same percentage since 2014. The domestic general government expenditure on healthcare was 63.085% which indicated the share of health expenditures subsidised by public sources. In 2015 the healthcare expenditure was €414 million. This was followed by a 12.5% increase of the allocated budget for health in 2016 resulting in €466 million (Azzopardi et al., 2017).

Among the number of comprehensive health services provided by the Maltese health system is the supply of free pharmaceutical products as regulated by the Social Security of 1987.⁴ In 2007, the distribution of free pharmaceuticals to entitled patients moved from centralized Government pharmacies located in five health centres and hospitals in Malta and Gozo to the private community pharmacies through the Pharmacy of Your Choice Scheme, (POYC). The transfer was intended to improve the pharmaceutical care service given to patients, and to eliminate the inconvenience of the patients having to attend to a regional health centre to pick up their medications every 2 months. Through the POYC scheme, patients could visit the community pharmacy of their own choice and collect their medications from the respective pharmacy. This allowed pharmacists in the community

³ Global Health Expenditure Database. Geneva: World Health Organization. (cited 2020 Aug 11)

⁴ Social Security Act 1987 [Internet]. Malta (cited 2020 Aug 11) Available from <http://justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=8794>

pharmacies to capture a good history of the current medications their patients were taking through the Government scheme allowing for improved safety and efficacy.⁵

1.3. Pharmacy of Your Choice (POYC) Scheme

A study in 2014 reported that 72.8% of the patients prefer the POYC scheme and received more benefits compared to the previous system of collection from government pharmacies (Xuereb et al., 2014). The POYC scheme distributes medications and medical devices to patients who are entitled according to the Schedule V and Schedule II of the Social Security Act.⁶⁷

1.3.1. Schedule V entitlement

In 1956 National Assistance Act was enacted, granting persons suffering from a chronic disease eligibility to medical assistance, notwithstanding financial resources. This Act empowered Malta's social security regulations. Through the Schedule V, patients who are suffering from a chronic condition listed in the Schedule V, are entitled to free medications available on the Government Formulary List. The Schedule V to date, consist of seventy-nine conditions (Appendix 1). The new Health Policy Strategy grants diabetic patients with a valid Schedule V a privilege for new medicines, blood sugar monitoring strips, sight

⁵ National Audit Office. Performance Audit An Analysis of the Pharmacy of Your Choice Scheme [Internet]. Malta (cited 2020 Aug 09).

⁶ Schedule V. Social Security Act 1987 [Internet]. Malta (cited 2020 Aug 11) Available from <http://justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=8794>

⁷ Schedule II. Social Security Act 1987 [Internet]. Malta (cited 2020 Aug 11) Available from <http://justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=8794>

glasses, free dental treatment, antibiotics, insulin syringes, aqueous cream, and rebates on telecare services.⁸

Patients who are entitled to free medications under the Schedule V are issued a yellow card which is not transferrable. The yellow card documents medicines and medical devices to which the card holder is entitled. The yellow card is a soft document which is kept by the patient. The POYC software documents an electronic version for each patient. Each pharmacy within the POYC scheme has access to the electronic documents of the patients registered under the respective pharmacy.

1.3.2. Schedule II entitlement

The Schedule II entitlement relates to the financial status and a means test of the respective patients. Patients with financial restrictions such as low-income group, unemployed, severely disabled, nuns and prisoners are eligible to a limited number of medicines, mainly for acute conditions, denoted as ‘pink card positive’ on the Government Formulary List (GFL).⁹ These patients are issued a pink card.

The pink card positive drugs has three categories: (A) items for acute use like those for conditions where treatment is short-term and a rapid onset of action is required; (C) items for chronic use which are indicated for recurring and ongoing conditions; and (B) items for both acute and chronic use depending on the illness.

⁸ Schedule V [Internet]. Malta: gov.mt.2020 (cited 2020 Aug 08). Available from: <https://deputyprimeminister.gov.mt/en/poyc/Pages/Schedule-V.aspx>

⁹ Medicines Approval Section [Internet] Malta: GOV.MT; 2020 (cited 2020 Aug 08). Available from URL: <https://deputyprimeminister.gov.mt/en/poyc/Pages/360%C2%B0-One-Stop-Shop-Service-Concept/Medicines-Approval/Introduction.aspx>

1.3.3. Government Formulary List (GFL)

The Government Formulary List (GFL) is comprised of medicinal products, vitamins, food supplements and borderline substances such as enteral feeds and parenteral foods. The pharmaceutical items are listed according to the International Non-proprietary Name (INN) of the medicinal products, the dosage form, the dosage strength, the indication category, and the classification according to the Anatomical Therapeutic Chemical (ATC) classification code. Each item has a designated prescriber criteria which includes the category of physicians who are authorised to prescribe each particular medicine. Medicines which can be issued to pink card holders according to Schedule II are specifically marked as “pink positive drugs”. Medicines which are regulated by a specific medicine protocol in terms of indication are denoted by "Medicine Protocol" (MP). Items such as the biologic drugs used in rheumatology are governed by a Medicine Protocol to ensure that these drugs are prescribed as second line drugs to traditional conventional disease modifying anti-rheumatic drugs, like methotrexate, in line with international guidelines.

The Government Formulary List is subdivided into two lists, the out-patient’s formulary and the hospital formulary. The out-patient’s formulary list consists of pharmaceutical products mapped to the corresponding chronic conditions as per schedule V and which are available and accessible within community. The hospital formulary lists pharmaceutical products available and accessible within the public hospital sector.

1.3.4 Registering within the POYC scheme

Patients entitled to free pharmaceutical items are required to register with a private community pharmacy of their own choice by filling in a registration form. Subsequently a POYC Scheme Membership Card specific to each patient is issued together with entitlement documents such as the Schedule V card (yellow card), the pink card and any approvals for special drugs such as Medicine Protocol drugs or narcotic drugs.¹⁰ Patients need to present the entitlement documents issued by POYC in addition to valid prescriptions and the patient's identity card.¹¹ The pharmacist within the community pharmacy registered within POYC accesses the POYC software, verifies the prescription and the entitlement documents, prepares and dispenses the items to the patient whilst offering pharmaceutical care accordingly.^{12,13}

¹⁰ Medicines Approval Section [Internet] Malta: GOV.MT; 2020 (cited 2020 Aug 08). Available from URL: <https://deputyprimeminister.gov.mt/en/poyc/Pages/360%C2%B0-One-Stop-Shop-Service-Concept/Medicines-Approval/Introduction.aspx>

¹¹ Prescriptions that are issued are valid for 6 months thus allows the patient to collect a two-month supply. Frequently Asked Questions [Internet] Malta: GOV.MT; 2020 (cited 2020 Aug 11). Available from URL: <https://deputyprimeminister.gov.mt/en/poyc/Pages/Schedule%20V/Frequently-Asked-Questions.aspx>

¹² Pharmacy Of Your Choice National Scheme [Internet]. Malta: gov.mt.2020 (cited 2020 April 28). Available from: <https://deputyprimeminister.gov.mt/en/poyc/Pages/Poyc-scheme.aspx>

¹³ Times of Malta. Pharmacies dispense €142m in state medicines in 10 years. [Internet] Malta: Times of Malta; 2017 Nov 22 (cited 2020 Aug 09). Available from URL: <https://timesofmalta.com/articles/view/pharmacies-dispense-142m-of-state-medicines-in-10-years.663771>

1.4 Rationale of the study

As of May 2020, approximately 170,968 patients were registered¹⁴ across 221 private community pharmacies around Malta and Gozo.¹⁵ These patients are dispensed medications through the POYC. An insight into an analysis of drug usage within the POYC scheme could highlight priority areas for pharmacist-led patient counselling, patient self-empowerment education sessions and relevant point of care testing initiatives which can be implemented by POYC pharmacies. Drug analysis may also be helpful in mitigating drug shortages.

1.5 AIM

The aim of the study is to analyse drug usage within the POYC system.

1.5.1 Objectives

The objectives of the study are to:

- i. gather data on drug usage within a POYC registered pharmacy
- ii. monitor changes in drug usage within specific classes of drugs
- iii. identify commonly used drugs within POYC schemes

¹⁴ The Malta Independent Online. 170,968 people using Pharmacy of Your Choice scheme. [Internet] Malta: The Malta Independent Online; 2020 May 06 (cited 2020 Aug 09). Available from URL: <https://www.independent.com.mt/articles/2020-05-06/local-news/170-968-people-using-Pharmacy-of-Your-Choice-scheme-6736222835>

¹⁵ Times of Malta. Pharmacies dispense €142m in state medicines in 10 years. [Internet] Malta: Times of Malta; 2017 Nov 22 (cited 2020 Aug 09). Available from URL: <https://timesofmalta.com/articles/view/pharmacies-dispense-142m-of-state-medicines-in-10-years.663771>

Chapter 2

Methodology

2.1 Study Design

This study was a descriptive, quantitative study, focusing on data on patient drug usage in POYC scheme.

2.2 Study Setting

The data was gathered from a community pharmacy in the northern region of Malta. The pharmacy opens 6 days weekly, from 8:30 am to 7pm Mondays to Fridays, and until 6:00 pm during Saturdays. To date, there are almost 1,400 patients registered with the pharmacy, taken into account the inactive patients.

2.3 Ethical Considerations

The University Research Ethics Committee (UREC) online form was filled out and the outcome of self-assessment resulted in no problems being known. The form was submitted to the FREC for record and audit purposes along with the study protocol and proposal. Approval was granted was upon the receipt of correspondence from FREC (Appendix 2).

2.4 Data Collection and Procedure

This section describes the methodology outlined in terms of patient eligibility, data collection and data handling.

2.4.1 Patient Selection

All POYC patients who were registered with the pharmacy by January 2017 were eligible for inclusion. Patients who have been inactive, which means that they were not dispensed any medications for at least 3 months and deceased patients were omitted from the study. The pharmacy has a patient database list documenting all registered patients, and their details such as identification card number and date of birth. As part of the operations of the pharmacy, all patients are assigned a file number which they use to order and to claim their medications. For the purpose of this study, patients were picked randomly using an online random number generator. In the event that the patient did not qualify for inclusion, another random number was generated until patient is eligible. This type of sampling was implemented since there is complete access to the files of the entire population. A total of 200 patients were included for data collection.

2.4.2 Data Collection

The study patients' information were accessed using the POYC main dispensing system using their identification card number and their date of birth. Data gathered included age and sex of patient, generic name of the drug, dosage strength, date dispensed and the quantity dispensed between 2017 and 2019 both years inclusive. Medical devices were not included. Warfarin was not included because its dose and quantity is frequently changed

thus it will be difficult to record. Drugs were coded based on their stock code in the POYC system. The data was entered onto Microsoft Excel 2013.

2.4.2.1 Data Sheet

The data sheet was composed of 2 sheets entitled “Demographics and History” and “Classification of Medications”.

2.4.2.2 Demographics and History

The contents of this sheet include the identifier and demographics of the patient such as the file number, age, and sex, and the dispensing history which includes the generic name of the drug, dosage strength, date dispensed and the quantity dispensed.

Demographics			Dispensed drug & Quantity		
1	Patient number	24		AMLOD 10mg tab	56
	Sex	M		BENDR 5mg tab	56
	Age	73		FENOF 200mg tab	56
				PERIN 4mg tab	120

Figure 2.1 Data sheet headers

The dispensing history of the patients reporting all the medications dispensed for each individual patient for each year between 2017 and 2019 was documented in a table format. Each year was divided into six columns since medications are collected every 2 months. Dangerous drugs which are dispensed every month were counted on a 2 month basis, for the purpose of this study.

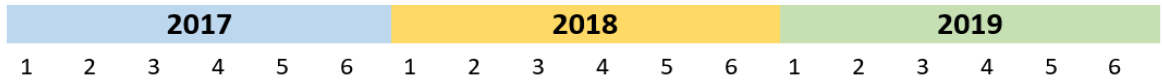


Figure 2.2 Dispensing history header

2.5 Classification of medications

The medications are classified into their respective therapeutic class based on the outpatients’ formulary list from the website of Ministry of Health. Drugs that were not part of the GFL were classified under “Other Disorders” (Table 2.1).

Table 2.1 Classification of Medications based on GFL

No.	Classification
1	Gastro-Intestinal System
2	Cardiovascular System
3	Respiratory System
4	Central Nervous System
5	Infections
6	Endocrine System
7	Obstetrics, Gynaecology, and Urinary-tract Disorders
8	Malignant disease and Immunosuppression
9	Nutrition and Blood
10	Musculoskeletal and Joint Diseases
11	Eye
12	Ear, Nose and Oropharynx
13	Skin
14	Anaesthesia
15	Other disorders

2.6 Identification of Potential Interaction of Drug Combinations

Potential drug interactions were investigated using Lexicomp® mobile application. The drug interaction feature of Lexicomp® was evaluated and validated by several studies and reported to have a specificity of 80-90% and sensitivity of 87-100%. It is considered to be one of the best drug interaction screening programs (Nusair et al., 2019). Information on mechanisms and the risk category were collected and tabulated to obtain the frequency.

For this study, only those interactions categorized as D and X were assessed. Those of categories A, B and C were excluded. The description of each risk category and their corresponding actions is presented in Table 2.2.

Table 2.2 Lexicomp® Categories of Drug-Drug Interactions

Category	Action Needed	Description
A	No known interaction	No evidence to support pharmacodynamic or pharmacokinetic interactions.
B	No known interaction	Evidence demonstrate that two drugs may interact with each other, but there is little to no clinical data to support it.
C	Monitor therapy	Evidence suggest that the two drugs may interact with each other in a clinically significant manner. The benefits of concomitant use of these two medications usually outweigh the risks. An appropriate monitoring plan should be implemented to avoid potential negative outcomes.
D	Consider Therapy Modification	Evidence suggests that the two medications may interact with each other in a clinically significant manner. Specific actions must be taken to minimize the toxicity resulting from concomitant use of the medications.
X	Consider Therapy Modification	The interaction of the two drugs is of clinical significance. The risks of concomitant use of these drugs usually outweigh the benefits and generally contraindicated.

Chapter 3

Results

3.1 Demographics of the sample

Out of 1,400 registered patients with the POYC scheme in a community pharmacy, drug usage data was obtained for 200 patients. Patient demographics collected include age and gender. The results showed that 53% of the population were females (n=107) and 47% were males (n=93), indicating a slightly higher number of female patients. The age was stratified as under 40 years, between 40 and 60, and over 61. Majority of the POYC patients (n=142) were identified to be senior citizens (60 years and older). The mean age of the patients was 66 years, ranging from 13 to 89 years.

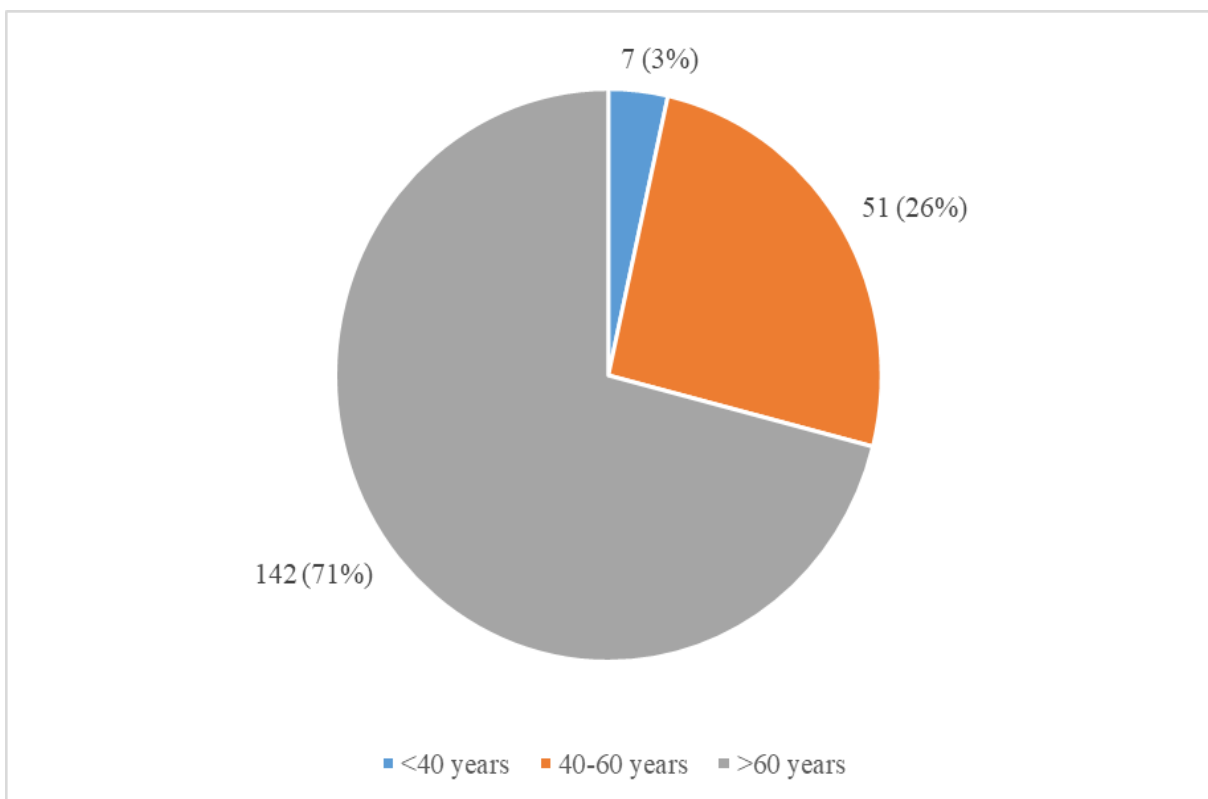


Figure 3.1. Patient Demographics: Age (N=200)

3.2. Number of Drugs Used According to Demographics

The number of drugs used per patient was correlated to gender and to age. One hundred twenty four patients were taking less than 5 drugs and 76 patients were on 5 or more drugs.

Table 3.1 Number of Drugs Used According to Gender and Age

Age	Male		Female	
	<5 drugs	≥5 drugs	<5 drugs	≥5 drugs
≤40	3		4	1
41-50	3	3	9	
51-60	11	6	13	5
61-70	15	18	19	5
71-80	14	12	22	15
>80	4	4	7	7

3.3 Number of Drugs Used According to Class

One hundred eight drugs prescribed in December 2019 were identified and grouped based according to the Government Formulary List classification. The 5 classes with the most number of drugs used were central nervous system (CNS) (n=30, 27.8%), cardiovascular (n=27, 25%), endocrine (n=10, 9.3%), respiratory (n=8, 7.4%), and gastrointestinal drugs (n=7, 6.5%) (Figure 3.2).

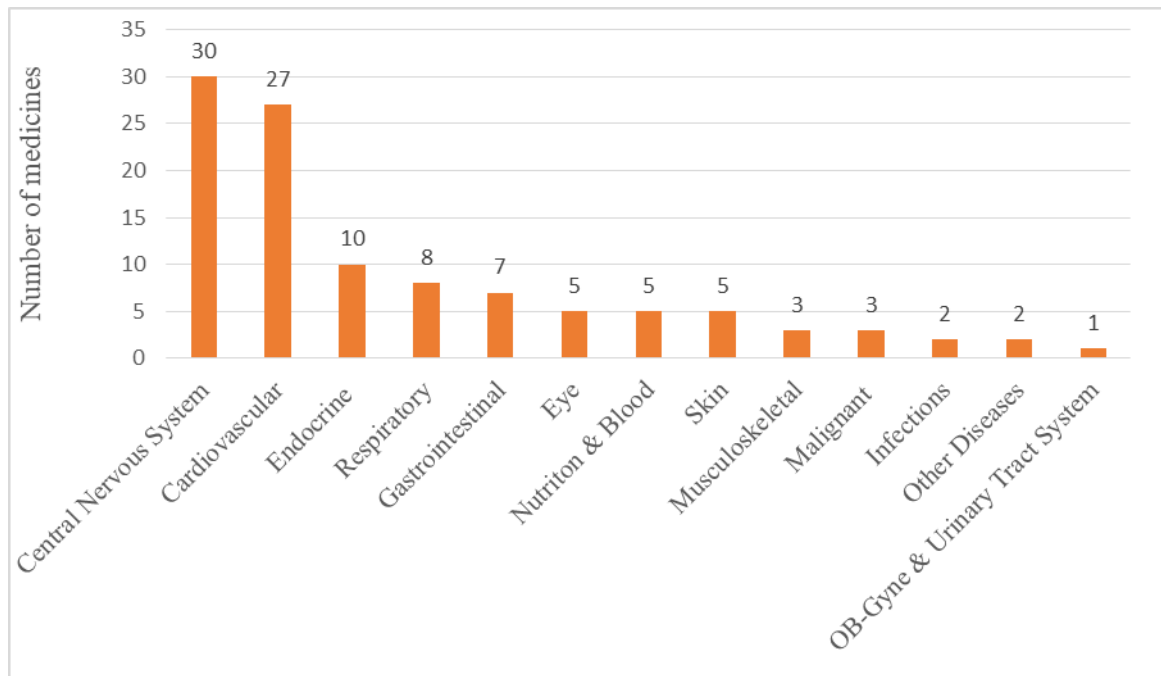


Figure 3.2 Number of Drugs Used According to Class

3.4. Distribution of drugs dispensed according to therapeutic system

The drugs dispensed within each therapeutic class and the number of patients who were taking them are presented in Table 3.2 -3.13.

The central nervous system presented the highest number of drugs dispensed. Five patients each were on amitriptyline, paracetamol and phenytoin respectively followed by 4 patients each who were on flupentixol, paroxetine, quetiapine, and valproate respectively (Table 3.2).

Table 3.2. Frequency of Central Nervous System Drugs Use

Drug name	Frequency	Drug name	Frequency
Amitriptyline	5	Sulpiride	2
Paracetamol	5	Benzhexol	1
Phenytoin	5	Clomipramine	1
Flupentixol	4	Clonazepam	1
Paroxetine	4	Donepezil	1
Quetiapine	4	Entacapone/Carbidopa/ Levodopa	1
Valproate sodium	4	Fluvoxamine	1
Carbamazepine	3	Lorazepam	1
Levetiracetam	3	Mianserin	1
Risperidone	3	Olanzapine	1
Venlafaxine	3	Phenobarbital	1
Bromazepam	2	Prochlorperazine	1
Fluoxetine	2	Ropinirole	1
Lamotrigine	2	Topiramate	1
Nortriptyline	2	Trifluoperazine	1

This class of drugs included the narcotics such as bromazepam, clonazepam and lorazepam which are relatively not commonly prescribed.

Table 3.3 summarises the number of patients on drugs within the cardiovascular system. The 5 most common drugs that were used by patients were simvastatin, amlodipine, aspirin, perindopril, and valsartan. Bezafibrate, co-amilozide, diltiazem, isosorbide dinitrate, and labetalol have the least number of patients using them (n=1).

Table 3.3. Frequency of Cardiovascular System Drugs Use

Drug name	Frequency	Drug name	Frequency
Simvastatin	74	Carvedilol	5
Amlodipine	62	Glyceryl trinitrate	4
Aspirin	56	Spiroonolactone	4
Perindopril	56	Rosuvastatin	3
Valsartan	53	Trimetazidine	3
Atorvastatin	34	Amiodarone	2
Bendroflumethiazide	32	Dipyridamole	2
Atenolol	27	Hydralazine	2
Enalapril	20	Bezafibrate	1
Bumetanide	13	Co-amilozide	1
Fenofibrate	10	Diltiazem	1
Doxazosin	8	Isosorbide dinitrate	1
Isosorbide mononitrate	8	Labetalol	1
Clopidogrel	6		

The top most commonly prescribed items are indicative that the cardiac conditions in this patient cohort are in line with recommended international standards. The low number of patients on clopidogrel could be attributed to the fact that clopidogrel is not recommended for longer than 1 year post acute coronary syndrome episode.

Five out of 10 drugs were used for diabetes mellitus within the endocrine system. Forty three patients were prescribed with metformin. Cabergoline and testosterone both have 1 patient taking them.

Table 3.4. Frequency of Endocrine System Drugs Use

Drug name	Frequency
Metformin	43
Gliclazide	25
Insulins	11
Levothyroxine	11
Vildagliptin	8
Glucagon	2
Hydrocortisone	2
Prednisolone	2
Cabergoline	1
Testosterone	1

Metformin is more commonly prescribed than gliclazide reflecting adherence to international guidelines putting metformin as first line treatment for diabetes mellitus type 2.

For drugs that act on the respiratory system, 10 patients were entitled to beclomethasone, budesonide and ipratropium. Salbutamol was the most commonly prescribed (n=30) (Table 3.5).

Table 3.5. Frequency of Respiratory System Drugs Use

Drug name	Frequency
Salbutamol	30
Beclomethasone	10
Budesonide	10
Ipratropium	10
Salmeterol	8
Fluticasone	4
Theophylline	2
Montelukast	1

Salmeterol and montelukast are protocol regulated within the Government Formulary List. The additional bureaucratic process to prescribe such items could be a reason as to why they are not commonly used.

With regards to the gastrointestinal system, omeprazole was the most frequently used drug (n=43). Two patients were prescribed with ursodeoxycholic acid. Ispaghula husk, antacid, lactulose, mesalazine, and sulphasalazine each have 1 patient using them (Table 3.6).

Table 3.6. Frequency of Gastrointestinal System Drugs Use

Drug name	Frequency
Omeprazole	43
Ursodeoxycholic acid	2
Antacid	1
Ispaghula husk	1
Lactulose	1
Mesalazine	1
Sulphasalazine	1

There is a prescribing tendency for omeprazole to be co-prescribed in addition to aspirin, or combination of aspirin and clopidogrel. It is also used in peptic ulceration in preference to ranitidine which is the only H₂ receptor antagonist available on the Government Formulary List.

From the data gathered on drugs for eye disorders, travoprost/latanoprost were prescribed for 9 patients, followed by timolol (n=7), and brinzolamide (n=3). Betaxolol and Brimonidine have the least number of users (n=2) (Table 3.7).

Table 3.7. Frequency of Drugs for Eye Disorders Use

Drug name	Frequency
Travoprost/Latanoprost	9
Timolol	7
Brinzolamide	3
Betaxolol	1
Brimonidine	1

With respect to drugs used with nutrition and blood use, folic acid was the most commonly used (n=5). There are 3 patients entitled to calcium lactate and 1 on ferrous fumarate.

Table 3.8. Frequency of Drugs for Nutrition and Blood Use

Drug name	Frequency
Folic acid	5
Calcium lactate	3
Alphacalcidol	2
Potassium chloride	2
Ferrous fumarate	1

Although the Government Formulary List includes calcium lactate and alphacalcidol, one must note that osteoporosis is not a schedule V condition and therefore osteoporotic patients are not entitled to calcium and vitamin D supplements available on the Government Formulary List. The use of these drugs within this patient cohort cannot be extrapolated as a reflection of osteoporosis in this patient cohort.

Table 3.9 summarises the frequency of use of drugs used to treat skin disorders. A total of 8 patients were entitled to drugs that are used for drugs and skin disorders. Three patients were on aqueous cream, 2 on hydrocortisone, and 1 on calcipotriol/betamethasone, emollient bath and mometasone.

Table 3.9. Frequency of Drugs for Skin Disorders Use

Drug name	Frequency
Aqueous cream	3
Hydrocortisone	2
Calcipotriol/Betamethasone	1
Emollient bath	1
Mometasone	1

In the study patient cohort, allopurinol was mostly used (n=6), followed by colchicine (n=3) among the drugs for musculoskeletal and joint diseases (Table 3.10).

Table 3.10. Frequency of Drugs for Musculoskeletal and Joint Diseases Use

Drug name	Frequency
Allopurinol	6
Colchicine	3
Diclofenac	1

This could be an indication of gout as a co-morbidity in this patient cohort, even though allopurinol could be used in gout secondary to oncology related conditions.

The frequency of use of drugs for immunosuppression and malignant use are reported in Table 3.11. Two patients were entitled to tamoxifen which is the first line treatment in local protocols for breast cancer.

Table 3.11. Frequency of Drugs for Immunosuppression and Malignant Disease Use

Drug name	Frequency
Tamoxifen	2
Ciclosporin	1
Mycophenolate	1

It is difficult to attribute the use of ciclosporin and mycophenolate to either malignant disease, rheumatology conditions or post transplant care.

Table 3.12 presents the frequency of drugs used for infections. Two patients are on Acyclovir and 1 on fluconazole.

Table 3.12. Frequency of Drugs for Infections Use

Drug name	Frequency
Acyclovir	2
Fluconazole	1

One must note that drugs used for infections and which are listed on the Government Formulary List are intended for use as co-adjunct treatment in immunosuppressed patients such as post transplant patients or oncology patients. Antibiotics used for acute short term infections are not usually dispensed free of charge to POYC patients.

Two drugs, namely the biologics adalimumab and tiopronin were classified under drugs for other disorders with 1 patient using each drug (Table 3.13).

Table 3.13. Frequency of Drugs for Other Disorders Use

Drug name	Frequency
Adalimumab	1
Tiopronin	1

It is interesting to note that no patient within the study cohort was reported as being on methotrexate which is usually co-prescribed with adalimumab for rheumatoid arthritis. However within this cohort, there are 1 patient each reported to be on sulphasalazine and mesalazine respectively. This could indicate that adalimumab is being used in addition to sulphasalazine as treatment of either rheumatoid arthritis or Crohns' disease or in addition to mesalazine in the management of Crohn's disease.

Potassium citrate (n=1) was the only drug under listed under obstetrics, gynaecology and urinary tract disorder drugs to be reported.

3.5 Trend of 10 Most Commonly Used Drugs across a 3-year Period

From the data gathered on the drugs and the number of patients taking them, the 10 most commonly used drugs and the usage trend between 2017 and 2019 were identified. An increase in the usage over the years for 8 out of 10 drugs was noted. The highest rise of tablets dispensed related to atorvastatin, with a 131.8% increase from 2017 (n=1,232) to 2019 (n=2,856). This was followed by omeprazole use which increased by 26.5%. The use of simvastatin was observed to decline, having 4,956 tablets dispensed in 2017 which went down to 4,564 in 2019. The pattern for aspirin use remained the same over the past 3 years. (Table 3.14).

Table 3.14 Trend of 10 Most Commonly Used Drugs Across a 3-year Period

Drug name	Quantity dispensed		% change
	2017	2019	
Simvastatin	4956	4564	-7.9%
Amlodipine	3584	4144	15.6%
Aspirin	3356	3356	0%
Perindopril	5160	5400	4.7%
Valsartan	3500	4032	15.2%
Metformin	8800	9670	9.9%
Omeprazole	3472	4392	26.5%
Atorvastatin	1232	2856	131.8%
Bendroflumethiazide	1736	1792	3.2%
Salbutamol	51	62	21.6%

3.6. Drug Combinations with Potential Interactions

The potential drug-drug interactions, their mechanism and category were investigated for the identified 76 patients with 5 or more than 5 medications. The results are presented in Table 3.15 by frequency. Overall, there were a total of 38 potential interactions detected. Thirty seven were classified as Category D and one was under Category X. The most frequent drug combination with potential interaction was amlodipine - simvastatin which appeared 15 times and was categorized as D. This was followed by combinations of vildagliptin - gliclazide, and omeprazole - clopidogrel (frequency=15) which were also category D. The drug combination which was identified as Category X was ciclosporin – simvastatin.

Table 3.15 Potential Interactions: frequency and risk category

Drug Combination	Mechanism of Interaction	Category	Frequency
Amlodipine - Simvastatin	Amlodipine may increase the serum concentration of Simvastatin	D	15
Vildagliptin - Gliclazide	DPP4 inhibitors may enhance the hypoglycemic effect of sulfonylureas	D	5
Omeprazole - Clopidogrel	Omeprazole may diminish the antiplatelet effect of Clopidogrel	D	5
Aspirin - Topiramate	Salicylates may enhance the adverse effects of carbonic anhydrase inhibitors	D	1
Ciclosporin - Simvastatin	Ciclosporin may increase the serum concentration of simvastatin	X	1
Ciclosporin - Mycophenolate	Ciclosporin may decrease the serum concentration of Mycophenolate	D	1
Atorvastatin - Phenytoin	CYP inducers (strong) may increase the metabolism of CYP3A4 substrates	D	1
Atorvastatin - Phenobarbital	CYP inducers (strong) may increase the metabolism of CYP3A4 substrates	D	1
Phenytoin - Atorvastatin	Phenytoin may decrease the serum concentration of HMG-CoA reductase inhibitors (statins)	D	1
Amiodarone - Simvastatin	Amiodarone may increase the serum concentration of simvastatin	D	1
Simvastatin - Diltiazem	Simvastatin may increase the serum concentration of Diltiazem. Diltiazem may increase the serum concentration of Simvastatin	D	1
Fluoxetine - Nortriptyline	Fluoxetine may enhance the serotonergic effect of tricyclic antidepressants	D	1
Carvedilol - Colchicine	P-glycoprotein inhibitors may increase the serum concentration of colchicine	D	1
Calcium lactate - Levothyroxine	Calcium salts may diminish the therapeutic effect of thyroid products	D	1
Fluoxetine - Risperidone	CYP2D6 inhibitors may increase the serum concentration of risperidone	D	1
Paroxetine - Amitriptyline	Paroxetine may enhance the serotonergic effect of tricyclic antidepressants	D	1

Chapter 4

Discussion

4.1 Demographics

Results from the study showed the differences in gender and age of the population. The number of females were slightly more than males. In terms of age, elderly patients who are over 60 years old comprised 71% of the population. The greatest number of patients was observed in age groups 61-70 and 71-80 with 57 and 63 patients, respectively. Only a few number of patients over 80 years was identified. Based on the 2019 news release of National Statistics Office-Malta, 24% of the estimated total population of Malta in 2018 aged from 60 years and above and there are more males than females but the difference is not that large.¹⁶

4.2 Number of Drugs Used According to Demographics

Older patients will in general consume a larger number of medications since they are bound to have more than one chronic disease. Polypharmacy, or the concurrent use of 5 or more medications is prevalent in this group (Duerden et al., 2013). Based on the present study, polypharmacy was detected in almost 4 out of 10 patients in POYC and it was more common in males. In contrast, other studies which were conducted in Malta found that there were more females who take 5 or more medicines than males. (Bugeja, 2013; Scicluna 2013). The presence of 5 or more drugs is more frequently noted in males at the age of 61-80, while in women, beyond 71 years old.

¹⁶ News Release. [Internet] Malta: National Statistics Office Malta; 2019 July 10 (cited 2020 Aug 16). Available from URL: https://nso.gov.mt/en/News_Releases/View_by_Unit/Unit_C5/Population_and_Migration_Statistics/Documents/2019/News2019_108.pdf

4.3 Number of Drugs Used According to Class

WHO Regional Office for Europe stated that 1 out of 4 people living in the European region is affected by a mental health disorder.¹⁷ European Health Interview Survey (EHIS) conducted in Malta reported that depression, anxiety, substance misuse, and dementia are the most common mental health disorders. Apart from these conditions, loneliness is also present in 1 out of 3 senior citizens. Drug utilization data of CNS drugs show that the most common disorders they were indicated for are chronic mood disorders, schizophrenia and chronic neurotic disorders, and psychosis.¹⁸ Most of the drugs identified upon data gathering were classified as CNS drugs, with an even distribution of frequency of use observed.

Cardiovascular diseases remain to be the top cause of mortality in the world, and also in Malta accounting to 32.5% of the deaths locally in 2014 (Gauci et al., 2018). Seven out of the 10 most commonly used drugs belonged to this therapeutic class. Of the 7 drugs, 2 were used for used for dyslipidemia. The findings of the present study was consistent with the results of another local study in 2013 in which cardiovascular drugs was the most commonly used therapeutic class of the patients. Simvastatin was the cardiovascular drug that was most frequently prescribed (Scicluna, 2013).

Drugs used for disorders of the endocrine system, particularly for diabetes mellitus which comprised 50% of the endocrine drugs, placed third on the frequently dispensed therapeutic

¹⁷ The European Mental Health Action Plan 2013-2020. [Internet] Malta: World Health Organization: 2015 (cited 2020 Aug 16). Available from URL: https://www.euro.who.int/__data/assets/pdf_file/0020/280604/WHO-Europe-Mental-Health-Acion-Plan-2013-2020.pdf

¹⁸ A Mental Health Strategy for Malta 2020-2030. [Internet] Malta: Ministry of Health: 2018 December (cited 2020 Aug 16). Available from URL: https://meae.gov.mt/en/Public_Consultations/MEH-HEALTH/Documents/Mental%20Health%20Strategy.pdf

class. In Malta, one in four persons over 60 years old is diagnosed with diabetes.¹⁹ Within the class, metformin was the most commonly prescribed for diabetes. The treatment recommendations for diabetes is presented in Malta National Strategy for Diabetes which stated that Metformin remains the first-line drug in diabetes mellitus. The recommended second-line therapy was the combinations using one or two additional oral drugs or an injectable drug such as insulins.¹⁹ This is consistent with what the British National Formulary recommendations. (BNF 2018, p.672)

There is an association with diabetes mellitus and cardiovascular disease, as diabetes mellitus is an independent risk factor for cardiovascular disease and vice versa (Leon & Maddox, 2015). Various studies have also shown the co-existence of hypertension and dyslipidemia (Chobanian et al., 2003; Johnson et al., 2004). Thus, drugs used for these diseases are frequently prescribed together. This is supported by the results of the present study and by another local study (Scicluna, 2013).

4.4 Trends of Most Commonly Used Drugs Across a 3-year Period

There was an increasing trend of usage for 8 out of 10 drugs. It was determined using the number of tablets dispensed. The addition of the drug to a patient or increase in the strength or frequency would lead to an increase of drug usage.

Simvastatin and atorvastatin are used in dyslipidemia. Atorvastatin had a 131.8% increase in usage from over a period of 3 years, which was the highest among all of the drugs. On

¹⁹ Diabetes: A National Public Health Priority 2015-2020. [Internet] Malta: Ministry of Health: 2014 (cited 2020 Aug 16). Available from URL: https://meae.gov.mt/en/Public_Consultations/MEH-HEALTH/Documents/NL-16-2014%20%20Diabetes%20A%20National%20Public%20Health%20Priority%202015-2020/Diabetes%20%20A%20Public%20Health%20Priority%20final%20document.pdf

the other hand, the usage of simvastatin was reduced by 7.9%. A study by Minard et al. in 2016 suggested that the dispensing pattern favoured atorvastatin and rosuvastatin in response to the rosuvastatin market entry and generic atorvastatin availability. In 2012, the Department of Health released a circular memo which announced the deletion of fluvastatin from the government formulary list. Those who were on fluvastatin were switched to atorvastatin.²⁰

Omeprazole is commonly used by older populations against a number of problems including gastro-protection against non-steroidal anti-inflammatory drugs and other drugs used for chronic diseases (Pham et al., 2006). The increased use of omeprazole might be attributed to the shift to omeprazole from ranitidine due to concerns of the presence of impurities nitrosamines in ranitidine products which may cause cancer.²¹

Long-term use of 75 mg aspirin is recommended by several guidelines for the secondary prevention of cardiovascular events (Huang et al., 2011). Chronic use of aspirin does not involve any increase nor reduction of the dose thus no change in usage has been observed.

4.5 Drug Combinations with Potential Interactions

Almost 40% of the identified potential drug interactions were of Amlodipine-Simvastatin combination. American Heart Association (AHA) stated that the maximum dose of simvastatin should be 20 mg if prescribed together with amlodipine. Doses of simvastatin

²⁰ DH Circular 54/2018DH 928/2018. Deletion of Fluvastatin and Changes in Statin Entitlement. [Internet]. Malta: gov.mt.2018 Jul 11 (cited 2020 Aug 17). Available from URL: https://deputyprimeminister.gov.mt/en/pharmaceutical/Documents/Circulars/2018/circular_54_2018.pdf

²¹ Circular P20/2019. EMA starts a review on ranitidine-containing products following detection of NDMA. [Internet]. Malta. 2019 Jul 20 (cited 2020 Aug 17). Available from URL: <http://www.medicinesauthority.gov.mt/file.aspx?f=4477>

higher than 20 mg predisposes the patient to a higher risk of unwanted muscle effects such as myalgia, myopathy and rhabdomyolysis (Wiggins et al., 2016). Among the 15 patients with amlodipine – simvastatin interaction, 3 were clinically significant as they were prescribed with amlodipine 10 mg and simvastatin 40 mg. This interaction was not of significance to 12 patients taking 20 mg or less simvastatin.

Other interactions involving simvastatin include combination with amiodarone, diltiazem, and ciclosporin all of which increases the serum concentration of simvastatin leading to increased susceptibility to adverse effects. All of these interactions are CYP3A4 enzyme mediated (Sathasivam & Lecky, 2008; Rowan et al., 2009). Atorvastatin combined with phenytoin or phenobarbital can also result to increased metabolism of atorvastatin. AHA recommends that other statins which are not metabolized by CYP3A4 enzyme can be considered such as fluvastatin, pravastatin or rosuvastatin (Wiggins et al., 2016). Rosuvastatin is on the formulary list while fluvastatin was previously available. On 2018, fluvastatin was deleted in the GFL due to international shortage.²² POYC can consider the addition of other statins to the formulary to avoid this interaction.

The significance of negative cardiovascular outcomes caused by the combination of omeprazole and clopidogrel was reported by several randomized trials (Pezalla et al., 2008; Ho et al., 2009; Evanchan et al., 2010). An opposite view was published in a study by Douglas et al. which stated that this interaction is minimum to no impact. In 2014, AHA released a guideline that pantoprazole is preferred if a proton pump inhibitor is warranted due to its reduced effects at the CYP2C19 enzyme (Kernan et al., 2014).

²² DH Circular 54/2018DH 928/2018. Deletion of Fluvastatin and Changes in Statin Entitlement. [Internet]. Malta: gov.mt.2018 Jul 11 (cited 2020 Aug 17). Available from URL: https://deputyprimeminister.gov.mt/en/pharmaceutical/Documents/Circulars/2018/circular_54_2018.pdf

Hypoglycemia induced by the interaction of vildagliptin and gliclazide is of importance. A meta-analysis showed that there is a 50% increased risk of hypoglycemia when adding vildagliptin to sulfonylureas. This is managed by reducing the dose of gliclazide and by frequently monitoring of blood glucose (Salvo, 2016). All diabetic patients under the POYC scheme are provided with glucose meters and glucose strips to be used for monitoring.²³

4.6 Potential Roles of Pharmacists

The setting of the POYC scheme gives the advantage of making the pharmacist accessible to the patient. Monitoring of drug therapy to prevent adverse drug reactions and to improve therapeutic outcomes of the patient can be performed.

Drug-drug interactions are known to have been prevented by community pharmacists (Bond et al, 2000). Incorporation of automatic detection of drug-drug interactions to the POYC software could be of even greater aid to pharmacists to perform interventions on such medication problems.

In one study, patients deem that provision of diagnostic testing is one of the most important extended professional services that the pharmacist can offer (Vella et al., 2015). POYC scheme also grants the potential to offer patient-centered point-of-care testing depending on the medications which the patient is entitled to. These may include medication review and checking for blood pressure, blood glucose, lipid profile and body mass index. This makes

²³ Falzon G. TVM. Free equipment and glucose sticks for diabetics receiving treatment. [Internet] Malta: TVM.com.mt; 2018 Apr 4 (cited 2020 Aug 17). Available from URL: <https://www.tvm.com.mt/en/news/free-equipment-and-glucose-sticks-for-diabetics-receiving-treatment/>

health check tests accessible to patients and results of which can also identify certain concerns. Outcomes of tests can verify if the current therapy is taking effect and may also uncover potential drug-drug interactions and adverse drug reactions, all of which could be discussed by the pharmacist both to the patient and the prescriber.

In another aspect, development of a national patient medication database would be helpful for instances when the patient goes to consultants in different specialties or when the patients buys over the counter medication in pharmacy. The latter suggests that pharmacists be authorised to utilise electronic records to be knowledgeable of the current and previous medications taken by the patient, enabling him/her to tailor the service provision.

4.7 Limitations of the Study

This study has potential limitations. The data obtained was only from one pharmacy, thus the results and conclusions does not represent the whole population of Malta. Due to the small sample size, estimates and trends that were generated were only for the most common medications that were dispensed. This study could have provided more concrete data interpretation and analysis if statistical analysis was employed.

4.8 Further Research

Further work in this area could include:

1. a large sample size and to get samples from each localities/districts of Malta is ideal to represent the whole population of Malta to capture the trends better.

2. administration of a questionnaire or face-to-face interviews to gather other data such as living situation, locality of residence, education level, family history, smoking and alcohol habits, physical activity as these will affect the trends of medication use of the patients and these their correlation to drug use can be analysed.
3. taking into consideration other pertinent data such as indication of the drug and other comorbidities can be collected as well.

4.9 Conclusion

The study captured drug usage data for patients registered with the POYC scheme in a community pharmacy. The number of drugs currently used by the patient were correlated to their demographics. Polypharmacy was noted to be more prevalent in the male population.

The classes which have the most number of drugs used were those used for the central nervous and cardiovascular system. The frequencies of drug use were identified for each drug and were tabulated. Simvastatin, amlodipine, aspirin, metformin and omeprazole were among the most commonly used drugs noted. The study also generated a usage trend of the 10 most commonly used drugs between 2017 and 2019, with atorvastatin reported to have the highest increase and simvastatin being the only drug noted to have a decrease in use.

Potential interactions of predominant drug combinations were detected and assessed according to their frequency and risk category. Overall, the findings of the study consistently suggest the impending role of community pharmacists in improving therapeutic outcomes of patients in the national health system.

References

Amber HS, Feroz S. Comparison of Health Care Delivery Systems: Pakistan Versus Germany. *i-Manager's Journal on Nursing* 2017 Feb;7(1):23-28.

Azzopardi-Muscat N, Buttigieg S, Calleja N, Merkur S. Health Systems in Transition: Malta Health system review. *European observatory on health system and politics* 2017; 19(1):16-18.

Bugeja A. Drug-drug interactions in repeat prescriptions at village dispensaries (bereg) in Malta. *Journal of Malta College of Family Doctors* 2013:22(1).

Bond C, Matheson C, Williams S, Williams P, Donnan P. Repeat prescribing: a role for community pharmacists in controlling and monitoring repeat prescriptions. *British Journal of General Practice* 2000; 50(453):271-275.

British National Formulary, 76th Edition (Sep 2018). London: British Medical Association and Royal Pharmaceutical Society of Great Britain.

Duerden M, Avery T, Payne R. Polypharmacy and medicines optimisation: Making it safe and sound. London: The King's Fund; 2013 p. 5

Evanchan J, Donnally MR, Binkley P, Mazzaferri E. Recurrence of acute myocardial infarction in patients discharged on clopidogrel and a proton pump inhibitor after stent placement for acute myocardial infarction. *Clin Cardiol* 2010;33(3):168-171.

Gauci D, England K, Calleja N. European Health Interview Survey (EHIS) 2014/15 Summary Statistics. 2018.

Ho PM, Maddox TM, Wang L, Fihn SD, Jesse RL, Peterson ED, et al. Risk of adverse outcomes associated with concomitant use of clopidogrel and proton pump inhibitors following acute coronary syndrome. *JAMA* 2009; 301(9), 937–944.

Huang ES, Strate LL, Ho WW, Lee SS, Chan AT. Long-term use of aspirin and the risk of gastrointestinal bleeding. *The American journal of medicine*. 2011 May 1;124(5):426-33.

Kernan W, Ovbiagele B, Black H, Bravata D, Chimowitz M, Ezekowitz M, et al. Guidelines for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke*, American Heart Association 2014;45(7):2160-2236.

Leon B., Maddox T. Diabetes and cardiovascular disease: Epidemiology, biological mechanisms, treatment recommendations and future research. *World Journal of Diabetes*. 2015;6(13):1246.

Minard LV, Corkum A, Sketris I, Fisher J, Zhang Y, Saleh A. Trends in statin use in seniors 1999 to 2013: time series analysis. *PLoS One*. 2016 Jul 19;11(7):e0158608.

Mortensen M, Falk E, Schmidt M. Twenty-Year Nationwide Trends in Statin Utilization and Expenditure in Denmark. *Circulation: Cardiovascular Quality and Outcomes*. 2017;10(7):2.

Nusair MB, Al-Azzam SI, Arabyat RM, Amawi HA, Alzoubi KH, Rabah AA. The prevalence and severity of potential drug-drug interactions among adult polypharmacy

patients at outpatient clinics in Jordan. *Saudi Pharmaceutical Journal*. 2020 Feb 1;28(2):155-60.

Pezalla E, Day D, Pulliadath I. Initial assessment of clinical impact of a drug interaction between clopidogrel and proton pump inhibitors. *J Am Coll Cardiol* 2008;52(12):1038-1039.

Pham C, Regal R, Bostwick T, Knauf K. Acid Suppressive Therapy Use on an Inpatient Internal Medicine Service. *Annals of Pharmacotherapy*. 2006;40(7-8):1261-1266.

Podesta M, Galea N, and Calleja N. (2019). Malta's changing demographics: projecting Malta's future health system demands to 2030. In Azzopardi Muscat, Cauchi and Melillo Fenech (Eds.), *Public Health in Malta: 1999 - 2019* (pp. 15-19). Malta: Malta Association of Public Health Medicine.

Rowan C, Brinker AD, Nourjah P, Chang J, Mosholder A, Barrett J, et al. Rhabdomyolysis reports show interaction between simvastatin and CYP3A4 inhibitors. *Pharmacoepidemiol Drug Saf* 2009;18(4):301-309.

Salvo F, Moore N, Arnaud M, Robinson P, Raschi E, De Ponti F, Bégaud B, Pariente A. Addition of dipeptidyl peptidase-4 inhibitors to sulphonylureas and risk of hypoglycaemia: systematic review and meta-analysis. *BMJ* 2016;353:i2231.

Scicluna D. Medication adherence practices among patients attending the primary health care medical consultant clinics in Malta. [dissertation]. Msida: Malta. Department of Pharmacy, University of Malta; 2013.

Sathasivam S, Lecky B. Statin induced myopathy. *BMJ* 2008; 337:a2286

Vella M, Grima M, Wirth F, Attard Pizzuto M, Sammut Bartolo N, Vella J, et al. Consumer perception of community pharmacist extended professional services. *Journal of Pharmaceutical Health Services Research* 2015; 6(2): 91-96.

Wiggins BS, Saseen JJ, Page RL 2nd, Reed BN, Sneed K, Kostis JB et al. Recommendations for Management of Clinically Significant Drug-Drug Interactions With Statins and Select Agents Used in Patients With Cardiovascular Disease: A Scientific Statement From the American Heart Association. *Circulation* 2016;134(21):e468-e495.

Xuereb M, Serracino-Inglott A, Azzopardi LM. Perception of pharmacists and patients of the Pharmacist-of-Your-Choice Scheme in Community Pharmacies [poster presentation]. Msida: Malta. Department of Pharmacy, University of Malta; 2014.

Abstract Submitted to FIP Conference 2020

Ruba JB, Grech L, Serracino-Inglott A. Analysis of Patient Drug Usage Trends in the POYC Scheme (Appendix 3)

Appendices

Appendix 1

The Schedule V Chronic Conditions

V1.0

July 2020

The Schedule V Chronic Conditions

The Fifth Schedule of the Social Security Act lists the diseases and conditions in respect of which free medicines are provided irrespective of financial position. These are as follows:

1. Malignant Diseases
2. Cardiovascular Diseases:
 - (a) Chronic Heart Failure
 - (b) Hypertension
 - (c) Ischaemic Heart Disease
 - (d) Cardiac Arrhythmias
 - (e) Peripheral Vascular Disease
 - (f) Cerebrovascular Disease
 - (g) Genetic Dyslipidaemia
3. Respiratory Diseases:
 - (a) Chronic Respiratory Failure
 - (b) Cystic Fibrosis
 - (c) Chronic Obstructive Pulmonary Disease
 - (d) Chronic Asthma
4. Digestive System Diseases:
 - (a) Gastro – Oesophageal Reflux Disease
 - (b) Gastric/Duodenal Ulcers
 - (c) Inflammatory Bowel Disease
 - (d) Coeliac Disease
 - (e) Diverticular Disease requiring Stoma Care
 - (f) Hirschprung's Disease
 - (g) Imperforate Anus
 - (h) Small Intestinal Failure
5. Liver Diseases:
 - (a) Chronic Liver Disease
6. Haematological Diseases:
 - (a) Inherited Bleeding Disorders
 - (b) Inherited Haemoglobinopathies
7. Nervous System Diseases:
 - (a) Epilepsy
 - (b) Parkinson's disease
 - (c) Myasthenia Gravis
 - (d) Multiple Sclerosis
 - (e) Motor Neurone Disease
 - (f) Trigeminal Neuralgia
 - (g) Huntington's Chorea
 - (h) Dementia
 - (i) Schizophrenia
 - (j) Psychosis
 - (k) Chronic Mood Disorders
 - (l) Chronic Neurotic Disorders
 - (m) Addiction Disorders
 - (n) Chronic Psychiatric Disorders starting in Childhood
 - (o) Chronic Eating Disorders
 - (p) Cerebral Palsy
 - (q) Narcolepsy
 - (r) Spinal Cord Pathologies

- (s) Congenital indifference to pain
 - (t) Neuromyelitis Optica
8. Renal Diseases:
- (a) Chronic Kidney Disease
9. Endocrine Diseases:
- (a) Diabetes Mellitus
 - (b) Addison's Disease
 - (c) Precocious Puberty
 - (d) Hypoparathyroidism
 - (e) Hypopituitarism
 - (f) Hypogonadism
 - (g) Enzyme Disorders
 - (h) Endometriosis and Adenomyosis
 - (i) Pituitary Adenomas
 - (j) Benign Prostatic Enlargement
10. Skin Diseases:
- (a) Psoriasis
 - (b) Chronic Immunobullous Disorders
 - (c) Congenital Ichthyosis
11. Infectious Diseases:
- (a) HIV/AIDS and HIV Related Diseases
 - (b) Hepatitis B & C
 - (c) Tuberculosis
 - (d) Hospital Acquired Infections
 - (e) Leprosy
 - (f) Polio and Post-Polio Syndrome
 - (g) Chronic Osteomyelitis
12. Rheumatic Diseases:
- (a) Rheumatoid Arthritis
 - (b) Paget's Disease
 - (c) Lupus Erythematosus
 - (d) Systemic Sclerosis
 - (e) Dermatomyositis/Polymyositis
 - (f) Polyarteritis Nodosa
 - (g) Spondyloarthritis
 - (h) Crystal Deposition Disease
 - (i) Polymyalgia Rheumatica
 - (j) Myalgic Encephalomyelitis
 - (k) Fibromyalgia
13. Metabolic Disorders:
- a) Inborn errors of Metabolism
14. Eye Diseases:
- (a) Glaucoma
 - (b) Vascular Disease of the Retina
15. Immunodeficiency:
- (a) Primary Immunodeficiency Disorder
 - (b) Secondary Immunodeficiency Disorder
16. Chromosome Disorders:
- (a) Down Syndrome
 - (b) Turner Syndrome
 - (c) Prader-Willi Syndrome
17. Gender Identity & Sex Characteristics Related Conditions

Appendix 2. Ethics Approval: Correspondence from FREC



John Bryan Ruba <john.ruba.19@um.edu.mt>

Registering study with Faculty Research Ethics Committee

FACULTY RESEARCH ETHICS COMMITTEE <research-ethics.ms@um.edu.mt>

3 August 2020 at 19:06

To: John Bryan Ruba <john.ruba.19@um.edu.mt>

Cc: Anthony Serracino Inglott <anthony.serracino-inglott@um.edu.mt>

Dear John Bryan Ruba,

Since your self-assessment resulted in no issues being identified, FREC will file your application for record and audit purposes but will not review it.

Any ethical and legal issues including data protection issues are your responsibility and that of your supervisor

[Quoted text hidden]

[Quoted text hidden]

Appendix 3. FIP Abstract



Pharmaceutical practice:
Health and medicines information
FIPSUB-1708 /

Analysis of Patient Drug Usage Trends in the POYC Scheme

John Bryan G. Ruba¹, Louise Grech¹, Anthony Serracino Inglott¹

¹Department of Pharmacy, Faculty of Medicine and Surgery, University Of Malta, Msida, Malta

My preferred method of presentation is: Poster Presentation

Please fill in the presenting author's organization: Department of Pharmacy, University of Malta

Background: The Pharmacy of your Choice (POYC) scheme is a national pharmaceutical service of Malta which provides free medicines and pharmaceutical devices for chronic diseases through the community pharmacies.

Purpose: To compile data on patient drug usage in POYC scheme.

Methods: All data was taken from a community pharmacy in Malta. POYC patients who are registered with the pharmacy were assigned a number and were picked randomly using an online random number generator. Patient details and drug usage history were taken by accessing the POYC software. Drugs were categorized into their respective therapeutic class based on the outpatients' formulary list from the Ministry of Health.

Results: Drug usage data was obtained for 73 patients, 38 male and 35 female patients (mean age 70 years). The 10 most commonly used drugs among POYC patients were Simvastatin (37), Amlodipine (23), Perindopril (22), Aspirin (21), Metformin (19), Valsartan (17), Omeprazole (16), Atenolol (13), Bendroflumethiazide (13), and Atorvastatin (12).

There has been an increase in the usage for 7 out of 10 drugs. The greatest rise observed was of Atorvastatin, with 1064 tablets dispensed in 2019 from 280 dispensed tablets in 2017, a 280% increase. Omeprazole and Valsartan have a 73% and 48.5% increase, respectively. The quantity dispensed for Simvastatin decreased from 2,632 in 2017 to 2,352 in 2018 and remained so in 2019. Dispensing of aspirin and bendroflumethiazide has been steady with 1256 and 728 dispensed tablets respectively for each year over the past 3 years.

Conclusion: The study captures a trends perspective of drug usage within the national health service.