RISK OF PHARMACIST PRESCRIBING WITH STATINS

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To my family. I love you endlessly.

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Abstract

Pharmacist prescribing has been shown to have positive clinical outcomes and is cost-effective. When used for primary prevention of atherosclerotic cardiovascular disease in patients with hypercholesterolaemia and/or diabetes mellitus type 2, statins reduce morbidity and mortality. Assessment of risks and benefits maximises effectiveness of statin treatment and enhances the advantages of pharmacist prescribing. The aim of this study was to determine the risks related to prescribing low- and moderate- intensity statins to patients aged 40-75 years with hypercholesterolaemia and/or diabetes mellitus type 2, both by medical practitioners and pharmacists.

Two self-administered questionnaires, one for medical practitioners and one for pharmacists, were developed, content-validated using modified Delphi method and reliability tested. After ethics approval, questionnaires were distributed by principal investigator, both in person and online to pharmacists and general practitioners. Data was analysed using SPSS. A regression model I was developed to determine the statistical difference, if any, of risks associated with prescribing of statins by medical practitioners and by pharmacists. In regression model II, the relationship between different predictors and total risk associated with prescribing of statins was analysed. Two protocols were put forward to be followed by pharmacists while potentially prescribing statins to patients with diabetes mellitus type 2 and hypercholesterolaemia.

The questionnaires were completed by 62 medical practitioners and 148 pharmacists. Pharmacists were supportive (83.1%) towards giving statin prescribing rights to pharmacists while medical practitioners opposed this scenario (67.7%). Factors that could ease the implementation of pharmacist prescribing in Malta, as perceived by both healthcare professionals, were patient privacy in a community pharmacy setting (73.8%)

and good inter-professional collaboration (72.8%). Comparison of the responses showed that both healthcare professionals were perceiving risks associated with prescribing of statins similarly, without any statistically significant differences. Medical practitioners were more familiar with guideline recommendations regarding statin prescribing when compared to pharmacists ($p<0.001$-0.033). Regression model I showed no statistically significant difference ($p=0.139$) in risks associated with prescribing of statins by medical practitioners and by pharmacists, while regression model II showed that healthcare professionals who were against giving statin prescribing rights to pharmacists rated the total risk of prescribing statins higher ($p=0.030$).

Pharmacists were in favour of expanding their scope of practice to prescribing of statins and results showed there are no increased risks associated with this activity, when compared to prescribing of statins by medical practitioners. Medical practitioner-pharmacist collaboration should be strengthened. Training courses aimed towards pharmacist prescribing should be organised in both undergraduate and postgraduate levels. Pharmacists should adopt a systematic approach to risk management in the eventuality of prescribing so risks associated with this activity can be reduced and patient outcomes optimised. The suggested protocols may reduce the risks associated with pharmacist prescribing and may standardise patient care. Risk reduction may increase support towards pharmacist prescribing. With identified factors and suggested protocols, this research can help policymakers in the smooth implementation of pharmacist prescribing of statins in Malta.

Keywords:

Pharmacist prescribing, risk of statin prescribing, risk management; pharmacists; medical practitioners

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List of Abbreviations

ASCVD	Atherosclerotic Cardiovascular Disease
BNF	British National Formulary
BP	Blood Pressure
CAD	Coronary Artery Disease
CKD	Chronic Kidney Disease
COPD	Chronic Obstructive Pulmonary Disease
CPG	Chronic Pain Grade
CV	Cardiovascular
CVD	Cardiovascular Disease
DIMM	Diabetes Intense Medical Management
eGFR	Estimated Glomerular Filtration Rate
EU	European Union
GFL	Government Formulary List
GP	General Practitioner
HbA1c	Glycated Hemoglobin
HCP	Healthcare Professional
HDL	High-density lipoprotein

HIV	Human Immunodeficiency
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
I-CVI	Item-Level Content Validity Index
LDL-C	Low-Density Lipoprotein Cholesterol
MUR	Medicines Use Review
NICE	National Institute for Health and Care Excellence
OTC	Over-The-Counter
SCORE	Systematic Coronary Risk Estimation
S-CVI	Scale-Level Content Validity Index
S-CVI/Ave	Scale-Level Content Validity Index/Average
S-CVI/UA	Scale-Level Content Validity Index/Universal Agreement
SPQ_{MedPr}	Statin Prescribing Questionnaire for Medical Practitioners
SPQ_{Pharm}	Statin Prescribing Questionnaire for Pharmacists
TC	Total Cholesterol
UK	United Kingdom
UTI	Urinary Tract Infection

Chapter 1

Introduction

This research aims to investigate the attitudes of medical practitioners and pharmacists in Malta towards potential pharmacist prescribing of statins to patients with hypercholesterolaemia and/or diabetes mellitus type 2, without previous atherosclerotic cardiovascular disease (ASCVD). Perceptions towards risks associated with prescribing of statins are assessed. By identifying the potential risks related to pharmacist prescribing and possible ways to ease the process of implementation of prescribing, this research can help pharmacists and other stakeholders to successfully implement pharmacist prescribing in Malta.

1.1 Models of Pharmacist Prescribing

The interventions of pharmacists have changed from being product-oriented to becoming more patient-oriented (Bishop et al, 2015; Schindel et al, 2017). In the light of this shift, one activity that has been added to pharmacists' scope of practice was prescribing. Models of pharmacist prescribing vary amongst different countries.

In the United Kingdom, supplementary and independent models of pharmacist prescribing are practiced.[1,2] Supplementary prescribing, established in 2003, is based on the voluntary cooperation between independent and supplementary prescriber.

1.Department of Health. Supplementary prescribing by nurses, pharmacists, chiropodists/podiatrists, physiotherapists and radiographers within the NHS in England. A guide for implementation [Internet]. London: Department of Health; 2005 [cited 2021 Mar 15]. Available from URL: https://webarchive.nationalarchives.gov.uk/20130124065910/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4110033.pdf

2. General Pharmaceutical Council. In practice: Guidance for pharmacist prescribers [Internet]. London: General Pharmaceutical Council; 2019 [cited 2021 Mar 15]. Available from URL: https://www.pharmacyregulation.org/sites/default/files/document/in-practice-guidance-for-pharmacist-prescribers-february-2020.pdf

A supplementary prescriber (previously known as dependent prescriber) can only manage the patients who were previously clinically assessed by an independent prescriber. A supplementary prescriber prescribes following a specific clinical management plan, which states conditions and limitations of prescribing.[2] The clinical management plan is the result of the agreement between independent and supplementary prescriber with the patient approval. A supplementary prescriber can also issue the repeat prescription with the right to adjust the dose or formulation of the drug.

An independent prescriber is responsible for the assessment and clinical management of the patients with undiagnosed or diagnosed conditions and can prescribe for any medical indication, within the area of expertise and clinical competence, including controlled drugs.[3,4,5] Exceptions are unlicensed cannabis-based medicinal products and three controlled drugs for the addiction treatment: cocaine, diamorphine and dipipanone.[2] Independent pharmacist prescribing in United Kingdom was approved in 2006.[3]

In the United States of America (USA), clinical pharmacists were authorised to prescribe medications by the Department of Veterans Affairs in 1995.[6] Laws differ from state to state. Two models of prescribing exist, collaborative and autonomous prescribing.[6]

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2. General Pharmaceutical Council. In practice: Guidance for pharmacist prescribers [Internet]. London: General Pharmaceutical Council; 2019 [cited 2021 Mar 15]. Available from URL: https://www.pharmacyregulation.org/sites/default/files/document/in-practice-guidance-for-pharmacist-prescribers-february-2020.pdf
3. Department of Health. Improving patients' access to medicines: A guide to implementing nurse and pharmacist independent prescribing within the NHS in England [Internet]. London: Department of Health; 2006 [cited 2021 Mar 15]. Available from URL: https://webarchive.nationalarchives.gov.uk/20130105033522/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4133747.pdf
4. Royal Pharmaceutical Society of Great Britain. Clinical governance framework for pharmacist prescribers and organisations commissioning or participating in pharmacist prescribing (GB wide) [Internet]. London: Royal Pharmaceutical Society of Great Britain; 2005 [cited 2021 Mar 15] Available from URL:https://www.palliativedrugs.com/download/clincgovframeworkpharm.pdf
5. The Government of the United Kingdom. Nurse and pharmacist independent prescribing changes announced [Internet]. London: The Government of the United Kingdom; 2012 [cited 2021 Mar 15]. Available from URL: https://www.gov.uk/government/news/nurse-and-pharmacist-independent-prescribing-changes-announced
6. Department of Veterans Affairs. Veterans Health Administration. Clinical pharmacy services. VHA handbook 1108 [Internet]. Washington, DC: Department of Veterans Affairs; 2017;11(1) [cited 2021 Mar 15]. Available from URL:https://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=3120

Collaborative prescribing relies on a formal agreement between a pharmacist and an independent prescriber and it enables the pharmacist to have a specific role in patient care, in addition to regular tasks performed. The prescriber and pharmacist negotiate to determine the pharmacist responsibilities and specific circumstances when pharmacists can carry out these additional duties.[7]

Autonomous prescribing includes both statewide protocols and unrestricted category-specific prescribing. It is less restrictive, but is limited to specific medications or categories of medications.[8] There is no need for partner prescriber and both categories apply to conditions which do not require specific, known or available diagnosis.

Statewide protocols are applied only to specific patient populations and are regulated by protocols issued by the state where individual pharmacists cannot negotiate the specific conditions. They are often aimed at solving public health problems, such as those related with naloxone, tobacco cessation products, oral contraceptives, tuberculosis skin testing and travel medications (Adams & Weaver, 2016).

Unrestricted category-specific prescribing is not restricted to specific patient populations and enables pharmacists to prescribe only certain medications such as fluoride supplements, immunisations and epinephrine auto-injectors. It is not regulated by state and pharmacists are usually obliged to prescribe as per recommendation of recent specific guidelines (Adams & Weaver, 2016).

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7. National Alliance of State Pharmacy Associations (NASPA). Collaborative Practice Agreements: Resources and More [Internet]. North Chesterfield, VA: NASPA; 2017 [cited 2021 Mar 15]. Available from URL: https://naspa.us/resource/cpa/
8. National Alliance of State Pharmacy Associations (NASPA). Pharmacist prescribing: Statewide Protocols and More [Internet]. North Chesterfield, VA: NASPA; 2018 [cited 2021 Mar 15]. Available from URL: https://naspa.us/resource/swp/#unique-identifier-statewide

In Canada, pharmacists could prescribe since 2007.[9] Depending on the province, pharmacists have different prescribing rights and training requirements and regulations vary.[10] The pharmacists' scope of practice ranges from only renewing the prescription for the continuum of care via ordering and interpreting laboratory tests, prescribing vaccines, making therapeutic substitutions to initiating a new drug from specific lists, either as part of collaborative agreement or independently.[10] Pharmacists in Alberta have the most prescribing rights, where they can initiate and change the drug treatment independently for any new drug, except the drugs covered with Controlled Drugs and Substances Act[11], including opioids, cannabinoids and barbiturates. Nunavut is the only province where pharmacists cannot even renew the prescription for the continuum of care.[10]

In New Zealand, pharmacists have had prescribing rights since 2013.[12] Pharmacist prescribers are designated prescribers and they can prescribe, under the collaborative prescribing model, medicines from a previously determined list of prescription medicines (Raghunandan et al, 2017). Pharmacists collaborate with other healthcare professionals and can initiate or modify medication therapy, within their area of expertise, to patients whose diagnosis has previously been determined.[13] Pharmacist prescribers can also order and interpret laboratory results, follow-up the response on treatment, and advise and inform patients.[13]

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9. Alberta College of Pharmacists. 2007-2008 Annual report [Internet]. Edmonton: Alberta College of Pharmacists;2008 [cited 2021 Mar 15]. Available from URL: https://abpharmacy.ca/sites/default/files/AR2007_08.pdf
10. Canadian Pharmacist Association. Pharmacists' Expanded Scope of Practice [Internet]. Ottawa: Canadian Pharmacist Association; 2018 [cited 2021 Mar 15]. Available from URL: https://www.pharmacists.ca/pharmacy-in-canada/scope-of-practice-canada/
11. Government of Canada. Justice Laws Website. Controlled Drugs and Substances Act [Internet]. Ottawa: Government of Canada; 2019 [cited 2021 Mar 15]. Available from URL: https://laws-lois.justice.gc.ca/eng/acts/c-38.8/page-1.html
12. New Zealand Ministry of Health. Pharmacist prescriber [Internet]. Wellington: New Zealand Ministry of Health; 2017 [cited 2021 Mar 15]. Available from URL: https://www.health.govt.nz/our-work/health-workforce/new-roles-and-initiatives/established-initiatives/pharmacist-prescriber
13. Pharmacy Council of New Zealand. Pharmacist Prescriber Scope of Practice [Internet]. Wellington: Pharmacy Council of New Zealand;2017 [cited 2021 Mar 15]. Available from URL: https://www.pharmacycouncil.org.nz/wp-content/uploads/Pharmacist-Prescriber-Scope-of-Practice-reviewed-Oct-17.pdf

The trend of pharmacist prescribing is spreading to other countries (Stewart et al, 2017), where pharmacists are gaining more rights and their authority of prescribing is increasing steadily (Stone et al, 2020). With this change comes the need to investigate the benefits of such an activity. The evidence can further guide the implementation of pharmacist prescribing (Stewart et al, 2017).

1.2 Benefits of Pharmacist Prescribing

Efficacy and safety of pharmacist prescribing should be carefully assessed. Besides the influence of pharmacist prescribing on clinical outcomes, the economic impact should also be explored.

1.2.1 Benefits in Clinical Outcomes

Meta-analysis by Weeks et al (2016) suggests that non-medical prescribers (pharmacists and nurses), practising in different settings including acute and chronic disease management, both primary and secondary care, are as effective as medical prescribers. Patient outcomes with non-medical prescribers are similar or better when compared to outcomes of medical prescribers regarding medication adherence, health-related quality of life and patient satisfaction. Findings from this meta-analysis also suggest that non-medical prescribers prescribed more drugs, used different types of drugs and higher doses when compared to medical prescribers.

Pharmacist prescribers reduced visits to the emergency department by 45.5% and hospital admissions by 13.2% (Kislan et al, 2016). Prescribing pharmacists in the University of North Carolina Medical Center were followed for two years and they improved patient health outcomes in diabetes mellitus and endocrine disorders, chronic pain conditions, cardiovascular disease, primary care patients, the elderly and different transplant patients, and reduced readmissions (Hawes et al, 2016). Tsuyuki et al (2016a) showed that pharmacist prescribers in Canada, during a three-month period, reduced future cardiovascular events by 21%.

A systematic review by Derington et al (2019) concluded that team-based care involving pharmacists is more effective than care without a pharmacist. In the review by Derington et al, pharmacist interventions ranged from making recommendations to physicians regarding medication management to prescribing. It should be noted that when the pharmacist is making a recommendation to a physician, a ceiling effect can exist in efficacy of pharmacist's interventions, because physicians can refuse certain recommendations due to different reasons (McLean et al, 2008). This is supported by Dalton et al (2019) who performed two randomised control trials in hospital in Ireland. They showed that when physicians gave the recommendation using STOPP/START criteria, acceptance and implementation of that recommendation by physician prescriber was 81.2% and 87.4% respectively. When pharmacists provided recommendation using STOPP/START criteria, acceptance and implementation by physician prescriber was 39.2% and 29.5% respectively. Pharmacists' recommendation for initiating statin treatment in patients with diabetes mellitus type 2, aged 40-75 for primary ASCVD prevention, was accepted by physicians in 90.2% of the cases, but statin was actually prescribed to 52.5% of the patients, while for others initiation was postponed until a future appointment (Vincent et al, 2020).

When hospital pharmacists prescribed in three hospitals, 0.3% error rate was recorded (Baqir et al, 2015). This is comparable to a study by Onatade et al (2017) who showed that, when pharmacists in hospital prescribed, the error rate was 0.2% affecting 2% of patients. In contrary, Ryan et al (2014) found that amongst junior doctors who prescribed in hospital, prescribing error was 7.5% of all prescribing items, which affected 36% of patients. Similar results were presented by Seden et al (2013) who showed that, amongst nine hospitals, when doctors prescribed (from junior to senior), prescribing error rate was 10.9% affecting 44% of patients. In a randomised control trial, the aim was to compare error rates associated with prescribing where intervention arm was pharmacist prescriber and control arm was a medical practitioner prescriber (Finn et al, 2020). Prescribing error rates in phase 1 where handwritten prescriptions were used, were 69% vs 4% affecting 95% vs 29% of the patients in medical practitioner and pharmacist arm respectively. In phase 2 where digital prescriptions were used, prescribing error rates were 21% vs 7% affecting 100% vs 62% of the patients in medical practitioner and pharmacist arm respectively.

One of the disease states where the benefits of pharmacist prescribing are very well documented is hypertension.

1.2.1.1 Hypertension

Pharmacist prescribing led to significant reduction of blood pressure (BP) (Green et al, 2008; Cohen et al, 2011; Franklin et al, 2013; Ip et al, 2013; Magid et al, 2013; Sease et al, 2013; Hirsch et al, 2014; McAlister et al, 2014; Tsuyuki et al, 2015; Tsuyuki et al, 2016a; Greer et al, 2016; Weeks et al, 2016; Kennelty et al, 2018). Collaboration between

a pharmacist prescriber and a primary health team, led to 93% more chances of achieving BP goals in a hypertensive patient (Brunisholz et al, 2018).

In the cluster-randomised trial, black male patrons of barbershops with uncontrolled hypertension were randomised either in a pharmacist prescriber-led group or in active control group consisting of visits to a physician and lifestyle interventions. After a period of six months, a mean decrease of systolic blood pressure was 21.6 mm Hg greater in the pharmacist prescriber-led group. In this group, 63.6% of the patients achieved target blood pressure below 130/80, versus 11.7% in the control group. Adherence to medication increased from 55% to 100% in the pharmacist prescriber-led group and 53% to 63% in the control group (Victor et al, 2018). The same group of patients were then followed for six months, with fewer pharmacist's visits to test long-term effects of pharmacist's interventions (Victor et al, 2019). A difference of 20.8 mm Hg, with the pharmacist prescriber-led group having greater decrease in blood pressure was recorded. More patients achieved target values of blood pressure in the pharmacist prescriber-led group compared to the active control group (68% vs 11%).

Margolis et al (2013) showed that pharmacist prescriber in combination with home blood telemonitoring significantly reduced BP over an 18-month period, where the pharmacist prescriber interacted with the patients for the first 12 months. During follow-up of 18 months, 15% more patients reached target BP in the pharmacist prescriber group, when compared to usual care. Margolis et al (2018) examined the sustainability of pharmacist prescriber interventions. Patients were followed-up for 54 months, where the pharmacist prescriber provided interventions during first 12 months. It was shown that the lower BP in the pharmacist prescriber-led telemonitoring group was sustainable for up to 24 months from the initial visit. After these 24 months, there were no observed differences between these two groups.

Amongst different implementation strategies to control elevated BP, team-based care approach including non-physician prescriber, was shown to provide the biggest reduction in systolic BP, according to a meta-analysis by Mills et al (2018). This approach enabled physicians to deal with more complex and urgent issues (Carter et al, 2012). It was shown that amongst non-physician prescribers, pharmacists decrease BP significantly more when compared to nurses (Carter et al, 2009). This statement is supported by a systematic review (Proia et al, 2014), which suggests that the addition of pharmacists to team-based care of patients with elevated BP, led to more patients with controlled BP, when compared to addition of other healthcare workers (nurses or others) to the team. When pharmacists were able to prescribe, independently or with the approval from the physician, a more effective BP reduction was observed than when pharmacists only provided advice and improved adherence (Proia et al, 2014).

It was estimated, that a hypothetical team-based care intervention for patients with hypertension, with pharmacists or nurses having prescribing authority, in a period of 10 years would reduce the number of people with uncontrolled hypertension by 4.7 million (around 13 % reduction). In patients older than 35 years, it would prevent 204 000 strokes, 130 000 myocardial infarctions, 638 000 cardiovascular events and around 165 000 cardiovascular disease (CVD)-related deaths (Dehmer et al, 2016).

1.2.1.2 Diabetes Mellitus

The addition of a pharmacist prescriber to the healthcare team who was managing patients with diabetes mellitus, led to significantly lower values of HbA1c (Cohen et al, 2011; Al Hamarneh et al, 2013; Franklin et al, 2013; Ip et al, 2013; Sease et al, 2013; McAdam-Marx et al, 2015; Greer et al, 2016; Tsuyuki et al, 2016a; Weeks et al, 2016; Brunisholz

et al, 2018) and fasting plasma glucose (Al Hamarneh et al, 2013). With pharmacist prescribers, patients were three times more likely to achieve target levels of HbA1c, when compared with the patients managed only by primary medical practitioners (Ip et al, 2013). These patients also had significantly lower 10-year CVD risk (Ip et al, 2013; Yu et al, 2013). When these patients had high BP, they were 87% more likely to achieve goals in both diabetes mellitus and BP, when compared to the usual primary healthcare team (Brunisholz et al, 2018).

Morello et al (2016) described Diabetes Intense Medical Management (DIMM) "Tune Up" Clinic where pharmacists collaborated with endocrinologists to manage patients with diabetes mellitus type 2. Patients with diagnosis of diabetes mellitus type 2 (HbA1c> 9%) were seen by a pharmacist in three 60-minute visits during a 6-month period. Pharmacists could initiate, adjust or discontinue any medication for diabetes or any related condition. In addition, pharmacists were able to order laboratory examinations and interpret results. During a 6-month period, HbA1c was checked twice (3- and 6-month check-up) and in the intervention group, HbA1c was significantly reduced than in the control group, on both occasions. In addition, more patients in the DIMM group achieved target fasting blood glucose. All of these outcomes were achieved without increasing medication regimen complexity, when compared to control group (Morello et al, 2018).

1.2.1.3 Dyslipidaemia

In a study by Tsuyuki et al (2016b), patients with uncontrolled dyslipidaemia from Canada, were enrolled in a randomised control trial. Pharmacists assessed CVD risk and low-density lipoprotein cholesterol (LDL-C) levels, prescribed medications, performed lifestyle interventions and follow-up. In a 6-month period, the intervention group with a

pharmacist prescriber had 43% of the patients who achieved LDL-C target goal, compared to 18% for the usual care group. Patients from the intervention group also had grater reduction in LDL-C values.

Other studies showed that pharmacist prescribing reduced levels of LDL-C and/or other lipids (Cohen et al, 2011; Ip et al, 2013; Sease et al, 2013; McAlister et al, 2014; Greer et al, 2016; Tsuyuki et al, 2016a; Weeks et al, 2016).

1.2.1.4 Other Conditions

Beahm et al (2018) showed that in the management of uncomplicated urinary tract infection (UTI), pharmacist prescribers had 89% of clinical cure rate and that there was very high satisfaction by patients. Pharmacists were also capable of identifying signs and symptoms of complicated conditions and referring patients to physicians.

Bruhn et al (2013) enrolled patients with chronic pain in United Kingdom. The authors compared pharmacist's medication review with or without pharmacist's prescribing, to usual care. The group with pharmacists' medication review and prescribing had statistically significant improvement in Chronic Pain Grade (CPG) intensity and disability. The group with pharmacist's medication review and referral to general practitioner (GP), together with pharmacist prescribing, had statistically significant improvements in total CPG score.

1.2.2 Economic Benefits

Besides the well-proven benefits on patient clinical outcomes, pharmacist prescribing should be assessed for its financial impact on healthcare costs. Total healthcare cost has been increasing over time due to the ageing population, polypharmacy, medication errors, new medicines and technological advancements (Dalton & Byrne, 2017). It is important that policy-makers direct healthcare resources to activities and treatments which are cost-effective (Gammie et al, 2017).

Tsuyuki et al (2015) showed that the full scope of pharmacist interventions regarding patients with hypertension (review of antihypertensive medications, assessment of cardiovascular risk and blood pressure control, patient counselling, prescribing and/or titrating of medications, laboratory testing and patients follow up) lowers the systolic blood pressure on average by 18.3 mmHg. The partial scope of interventions (patient counselling and education, diagnostics, referrals and interventions), when pharmacists are not able to prescribe, also improves the control of systolic blood pressure, but the decrease is around 7.6 mmHg (Santschi et al, 2014). Cost-effectiveness analysis of pharmacists providing full scope of interventions in treatment of patients with hypertension in comparison with usual care showed that full scope of interventions offered more cost savings (Marra et al, 2017). During a 30-year time period, pharmacist management of patients with hypertension using full scope of interventions was economically dominant when compared to usual care and estimated discounted cost savings of $6 000 per individual were calculated (Marra et al, 2017).

This would result in 953 000 life-years saved and, if applied to half of the patients with poorly controlled hypertension in Canada, this approach would save $15.7 billion.[14] Involvement of pharmacist prescribers can significantly reduce cost (McAdam-Marx et al, 2015; Michalets et al, 2015; Brown et al, 2016; Derington et al, 2019).

Some of the estimated savings are: $691 200 per year, pharmacist prescriber-led smoking cessation (Manolakis & Skelton. 2010); $74 906 per year, management of 95 patients with diabetes mellitus type 2 in a 2-year period (Sease et al, 2013); $2.4 billion during 10-years period, care for the patients with the hypertension (Dehmer et al, 2016) and $51.1 million in a period of 5 years, management of uncomplicated UTI (Sanyal et al, 2019).

Hirsch et al (2017) estimated that in the DIMM "Tune-Up" Clinic, from a health system perspective, decrease in medical cost due to improvement in HbA1c was $8 793 per DIMM patient compared to $3 506 per patient who was provided standard primary care. Return of investment was $9.01 on every dollar spent. Total estimated cost of DIMM patients was lower and risks for diabetes-related complications were reduced over a 2-, 5- and 10-year period.

Other studies evaluated the cost related to pharmacist-physician collaborative practice model when pharmacist had authority to initiate, adjust or discontinue medications for patients with diabetes mellitus type 2 (Franklin et al, 2013; Yu et al, 2013). Franklin et al (2013) showed that addition of the pharmacist to the diabetes-team resulted in cost savings per patient of $421.01.

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14. Broadstreet Health Economics & Outcomes Research. Improving health and lowering costs: Benefits of pharmacist care in hypertension in Canada [Internet]. Ottawa (ON): Canadian Pharmacists Association; 2017 [cited 2021 Mar 15]. Available from URL: https://www.pharmacists.ca/cpha-ca/assets/File/cpha-on-the-issues/Benefits_of_Pharmacist_Care_in_Hypertension_EN.pdf

Yu et al (2013) compared patients with a pharmacist prescriber (enhanced group) and a control group with patients having a primary care physician only, in the management of diabetes mellitus type 2. The enhanced group had lower cost per patient in a 10-year period ($35 740 vs. $44 528) and more life years saved (8.9 vs. 8.1).

1.3 Views of Patients and Public on Pharmacist Prescribing

Research about effectiveness and safety of pharmacist prescribing aims to support implementation of this type of prescribing throughout the world. Studies examining views and attitudes of patients and public are also very important because they can identify different factors, which support or oppose pharmacist prescribing. Understanding these views, pharmacists can overcome barriers, improve the service, better promote and educate stakeholders and improve implementation of pharmacist prescribing (Eckhaus et al, 2021).

1.3.1 Patients' Views on Pharmacist Prescribing

Patients were highly satisfied with the service provided by pharmacist prescribers in the primary care, mental health, contraception, Human Immunodeficiency (HIV) prophylaxis and cardiology (Stewart et al, 2008; Stewart et al, 2011; Tinelli et al, 2013; Buist et al, 2019; Hindi et al, 2019; Lutz et al, 2020; Zhu et al, 2020; Eckhaus et al, 2021; Speirits et al, 2021). Patients viewed the pharmacist as a drug expert (McCann et al, 2012a; Hindi et al, 2019) and thought that all the necessary and detailed information was given to them

during consultation (Stewart et al, 2008; McCann et al, 2012a; Speirits et al, 2021). Pharmacists were thought to be thorough and approachable (Stewart et al, 2011; Hindi et al, 2019). Patients were satisfied with the prolonged consultation time (McCann et al, 2012a; Hindi et al, 2019) and felt to have more control over their disease management plan (McCann et al, 2012a). Patients appreciated opportunity to ask questions and thought that involvement of pharmacist independent prescriber was beneficial for them and reduced their stress (Hindi et al, 2019; Speirits et al, 2021).

Gerard et al (2012) reported that patients were more likely to visit a pharmacist prescriber or personal GP, compared to any available GP. This can probably be explained with the good relationship patients have with the pharmacist prescriber and the fact they trust him/her (Tinelli et al, 2013; Hale et al, 2015). Patients would also recommend pharmacist prescribers to others (Stewart et al, 2011; Hale et al, 2015).

Patients felt that care provided by pharmacist prescriber was no different than usual care (Tinelli et al, 2013; Hale et al, 2015) and that safety related to prescribing was the same as with the GP (Stewart et al, 2011; Tinelli et al, 2013). Amongst prescribing by pharmacists and usual care, patients reported no difference in disease control, support for adherence and access (Tinelli et al, 2013).

In Australia, two different settings of collaborative doctor-pharmacist prescribing were set up to examine attitudes of patients towards implementation of pharmacist prescribing, and 93% of patients agreed to see the pharmacist prescriber regularly for management of their disease or condition (Hale et al, 2015).

Some studies assessed patients' experience in pharmacist prescribing concerning specific diseases or conditions. Steward et al (2018) enrolled patients with UTI, impetigo and chronic obstructive pulmonary disease (COPD) and concluded that patients were highly

satisfied with the treatment, provided care and quick and efficient access. In a hypertension clinic with pharmacist supplementary prescribers, 57% of patients thought that standard of care was better than with usual care and 76% said that their knowledge and understanding of the condition has improved while 92% agreed that pharmacists should supplementary prescribe (Smalley, 2006). A study from Canada enrolled patients who visited pharmacy for minor illnesses (Mansell et al, 2015). Patients were satisfied with both efficacy and safety of treatment initiated by pharmacist prescribers. Patients opted for this kind of service because it was convenient and they had trust in the pharmacist prescriber. Hill et al (2014) conducted an interview amongst patients attending addiction services in Scotland. Ninety-seven percent of the patients said that if they can choose which healthcare professionals they wish to consult, they would chose a pharmacist and 96% thought that pharmacists have good communication skills and are very capable. McKeirnan and MacLean (2018) showed that patients were willing to access pharmacist prescribing for minor ailments and conditions, if that service would being offered in rural areas in Washington state. Patients who had appointments with pharmacist independent prescribers in post-myocardial infarction left ventricular systolic dysfunction clinic reported benefits of multidisciplinary team, that pharmacist consultations helped them to understand better their condition and treatment, and that pharmacist provided more information compared to usual care (Speirits et al, 2021).

A review article by Famiyeh and McCarthy in 2017 shows that patients were highly satisfied with communication, service received and time of appointment, which referred to availability of pharmacist, duration of consultation and locality of the pharmacy. Patients reported increased access to medications and that their relationship with the pharmacist became stronger.

In a systematic review by Jebara et al (2018), patients were supportive towards pharmacist prescribing stating increased access to healthcare professionals and improved use of pharmacists' skills and knowledge.

Patients felt that the multidisciplinary team's care, which includes pharmacist prescribers, is an ideal option for the management of their health (McCann et al, 2012a; Speirits et al, 2021). Patients felt (65%, Stewart et al, 2008 and 69.6%, Stewart et al, 2011) more confident that their medical practitioner establishes the initial diagnosis or manage worsened or more complex conditions (McCann et al, 2012a). One reason for this is the excessive lack of awareness of pharmacist prescribing and training required to become a prescriber (McCann et al, 2012a).

Patients expressed their concerns regarding pharmacists' limited access to patient medical records (Famiyeh & McCarthy, 2017; Jebara et al, 2018), narrow pharmacists' diagnostic skills (if not prescribing collaboratively) and pharmacists' responsibility and lack of reimbursement (Jebara et al, 2018), lack of adequate training on specific drug treatment, like for example, HIV treatment (Lutz et al, 2020), organisational issues and especially lack of additional staff (Famiyeh & McCarthy, 2017; Jebara et al, 2018), patient health and cost of the treatment (Eckhaus et al, 2021) and insufficient privacy within a community pharmacy setting (Stewart et al, 2011; Zhu et al, 2020; Eckhaus et al, 2021). In their review article, Famiyeh and McCarthy, (2017) reported that patients were not worried about lack of privacy.

1.3.2 Public Views on Pharmacist Prescribing

The public supported pharmacists prescribing (Stewart et al, 2009; Bishop et al, 2015; Khan et al, 2017; Irwin et al, 2019). In studies done locally, public support towards pharmacist prescribing changed from 47% (Wirth et al, 2010) and 41% (Tabone et al, 2013) to 69% (Vella et al, 2015). The public agreed that it would be convenient for patients to have medicines prescribed in a pharmacy, with increased access to medicines and thought that pharmacists should have access to patient medical records prior to prescribing (Steward et al, 2009; Famiyeh et al, 2019). In a study by Famiyeh et al (2019) in Canada the public was not aware that pharmacists can prescribe. Irwin et al (2019) reports that public was not familiar with required education and training.

Pharmacists would be supported to prescribe in certain situations such as prescribing in emergency situations, prescribing for chronic conditions (Perepelkin, 2011; Khan et al, 2017, Jebara et al, 2018) and renewing of prescriptions (Perepelkin, 2011; Kelly et al, 2014; Famiyeh & McCarthy, 2017, Jebara et al, 2018; Famiyeh et al, 2019).

When it comes to more complex interventions, like changing the dose or dose frequency, the public was not supportive of pharmacists prescribing (Famiyeh et al, 2019). Perepelkin (2011) reports that 40% of interviewed public supported pharmacists to change the dose and 19% to diagnose new illnesses and prescribe new drugs. The public thought that pharmacists are as knowledgeable as doctors to prescribe medicines (31%) and that pharmacists could prescribe the same range of medicines as doctors (25%) (Stewart et al, 2009). This opposes the view of the public from more recent studies where it is reported that pharmacists should prescribe for chronic conditions (Famiyeh & McCarthy, 2017; Khan et al, 2017, Jebara et al, 2018) and for minor illnesses (Famiyeh & McCarthy, 2017).

In a national survey in Canada[15] in 2015, the public thought that pharmacists play a central role in the healthcare system (82%). The public agreed that in case of prescribing for minor illnesses, the overload of emergency rooms and walk-in clinics would be reduced (85%). They thought that pharmacists have enough knowledge and expertise to deal with more complex assignments, rather to just fill-in the prescriptions (85%) and that pharmacist should be part of the healthcare team in the care of patients with chronic conditions and that, through that involvement, the best care to patients would be provided (84%). The public stated that patients' quality of life would improve (82%) and that medical practitioner-pharmacist collaboration would decrease total healthcare costs (79%).[15]

The public showed concern about safety of prescribing (Irwin et al, 2019), privacy during consultation with a pharmacist prescriber and the lack of appropriate support for pharmacist prescribing, including limited access to medical records and lack of additional staff (Famiyeh & McCarthy, 2017) as well as lack of time (Irwin et al, 2019).

Some of the concerns of the patients and public were related to the potential risks of safety associated with pharmacist prescribing. Since risk is associated with any pharmacist's activity and any drug treatment, it should be further discussed.

15. Canadian Pharmacists Association (CPhA). Pharmacists in Canada: A national survey of Canadians on their perceptions and attitudes towards pharmacists in Canada [Internet]. Ottawa: CPhA; 2015 [cited 2021 Mar 15]. Available from URL: http://www.pharmacists.ca/cpha-ca/assets/File/news-events/PAM2015-Poll.pdf

1.4 Risk Considerations in Pharmacy

Relying on the available information, people are taking risks to live their lives, create their values and deal with challenges (Zinn, 2019). There is no universally accepted definition of the risk (Aven & Renn, 2009; Aven, 2010; Aven et al, 2011). In most definitions, common elements of risk are an event, a consequence in terms of an outcome and probability, where Aven (2010) suggests that probabilities should be replaced with the uncertainties. Aven suggests a definition where "risk is uncertainty about the event and uncertainty about outcome and its severity with respect to something valuable to humans" (Aven & Renn, 2009). The ICH guideline Q9 on quality risk management defines risk as the "combination of the probability of occurrence of harm and the severity of that harm".[16] Risk exists objectively in the world, it is not bound to its perception (Aven et al, 2011), indicating that even if person is not aware of some specific risk, risk will still exist. Risk perceptions are subjective and intuitive (Wilson et al, 2019) and they are influenced by the individual's knowledge (Zhu et al, 2016; Benítez-Díaz et al, 2020; Chen et al, 2020) or emotions (Lanciano et al, 2020; Oh et al, 2020). Not all will assign the same probability of some potential harm or comprehend the same level of seriousness (Aven et al, 2011).

Pharmacists need to be aware that it is impossible to reduce the risk of their activities to 'zero' and that some amount of risk needs to be present (Bush et al, 2005, Interrigi et al, 2017).[17]

16.European Medicines Agency (EMA). ICH guideline Q9 on quality risk management [Internet]. London: EMA; 2015 [cited 2021 Mar 15]. Available from URL: https://www.ema.europa.eu/documents/scientific-guideline/international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-use_en-3.pdf

17. National Health Service (NHS); Black Country Partnership NHS Foundation Trust. Clinical Risk Management [Internet]. London: NHS; 2019 [cited 2021 Mar 15]. Available from URL: https://www.bcpft.nhs.uk/documents/policies/r/1079-risk-management-clinical/file

Regarding drug treatments, various stakeholders are included, like patients, pharmacists, medical practitioners, carers or family members, regulatory authorities, and different perceptions of the risk exist depending upon each stakeholder involved in an individual's drug treatment.[16] The protection of the patient by minimising the risk should be of the most importance (Lotlikar, 2013). Fujita et al (2019) indicates that good-quality healthcare nourishes patient safety. The responsibility of the pharmacist is to try to maximise the benefit of a drug treatment while minimising the potential harm.

1.4.1 Clinical Risk Management with Respect to Statin Prescribing

Healthcare organisations, using a risk management process, are proactively taking care of patient safety (Suprin et al, 2019).[17,18] A risk management process also protects healthcare organisations and ensures its normal functioning.[18] Clinical risk management aims to determine, investigate and prevent risks in patient management using a systematic approach (Weingessel et al, 2017).

The risk management process should be personalised to the patient.[17] In the case of pharmacists prescribing statins, the risk management process can be explained as follows (Figure 1.1):[18]

16.European Medicines Agency (EMA). ICH guideline Q9 on quality risk management [Internet]. London: EMA; 2015 [cited 2021 Mar 15]. Available from URL: https://www.ema.europa.eu/documents/scientific-guideline/international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-use_en-3.pdf

17. National Health Service (NHS); Black Country Partnership NHS Foundation Trust. Clinical Risk Management [Internet]. London: NHS; 2019 [cited 2021 Mar 15]. Available from URL: https://www.bcpft.nhs.uk/documents/policies/r/1079-risk-management-clinical/file

18. Government of Western Australia; Department of Health. Clinical Risk Management Guidelines: A best practice guide [Internet]. Perth: Department of Health;2019 [cited 2021 Mar 15]. Available from URL: https://ww2.health.wa.gov.au/-/media/Files/Corporate/general-documents/Quality/PDF/WA-Health-Clinical-Risk-Management-Guidelines.pdf

Risk identification - identification of all the possible risks related with the established scenario of pharmacist prescribing of statins. [16,18] The aim is to identify as much different risks as possible (Simsekler et al, 2018). Some of the risks when prescribing statins could be: incorrect dose of statin, wrong choice of statin, increased incidence of interactions and side-effects.

Risk analysis - understanding the identified risks, the ratings and evaluation of controls to minimise the risks (Hansson & Aven, 2014). In the scenario of statin prescribing, risk factor 'increased incidence of interactions' can have different consequences for the patient, depending on whether the interaction is clinically significant or not, type and dose of statin used, as well as patient's characteristics and other medical conditions (Wiggins et al, 2017). As a consequence, plasma concentrations of the statin can be low or high which further implies lack of therapeutic effect or statin side-effects occurrence (Gravatt et al, 2017). Controls to minimise the risks could be following of the protocols for prescribing or checking for the interactions every time prior prescribing.

Risk evaluation – risks are evaluated according to their importance (Suprin et al, 2019). Risk evaluation implies prioritising risks and realising which risks require modification (avoid the risk, improve risk control or share or transfer the risk).[18] It is important to identify the risks which can harm the patient, for example incorrect dose of statin in patients with chronic kidney disease (CKD). Other risks require awareness and no action is needed, for example in the case of a clinically insignificant interaction (Wiggins et al, 2017).

16.European Medicines Agency (EMA). ICH guideline Q9 on quality risk management [Internet]. London: EMA; 2015 [cited 2021 Mar 15]. Available from URL: https://www.ema.europa.eu/documents/scientific-guideline/international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-use_en-3.pdf

18. Government of Western Australia; Department of Health. Clinical Risk Management Guidelines: A best practice guide [Internet]. Perth: Department of Health;2019 [cited 2021 Mar 15]. Available from URL: https://ww2.health.wa.gov.au/-/media/Files/Corporate/general-documents/Quality/PDF/WA-Health-Clinical-Risk-Management-Guidelines.pdf

It is important to clearly distinguish the type of risk, because any action associated with potential mitigation can be time consuming or unnecessary if a low risk is mistakenly taken for high (Simsekler et al, 2018). In contrary, serious harm can happen to a patient.

Risk treatment (reduction) - development of solutions to treat risks which are unacceptable (Lotlikar, 2013) by decreasing the probability and severity of the risk.[16] Different actions can be applied to those risks which can harm the patient. Some of the ways to treat the risk can be avoiding the activity which leads to risk, like stopping simvastatin while patient is on erythromycin (Gravatt et al, 2017), improving patient adherence by explaining benefits of statin treatment as well as educating patients about side-effects, their frequency and seriousness (Fung et al, 2010), identifying the patients at increased risk of side-effects and manage them accordingly, like prescribing reduced statin dose or monitor them more frequently (Ramkumar et al, 2016; Gravatt et al, 2017) or in case of the clinically significant interaction choosing other statin which does not interact significantly (Gravatt et al, 2017; Wiggins et al, 2017).

Understanding the risk will enable a thorough risk assessment, risk management and risk communication (Aven et al, 2011).

Communication and consultation should be included in every step of clinical risk management process (Figure 1.1).[18] Without effective communication different stakeholders would not be aware of benefits of clinical risk management neither will they comprehend their own roles in this process.[18]

16.European Medicines Agency (EMA). ICH guideline Q9 on quality risk management [Internet]. London: EMA; 2015 [cited 2021 Mar 15]. Available from URL: https://www.ema.europa.eu/documents/scientific-guideline/international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-use_en-3.pdf

18. Government of Western Australia; Department of Health. Clinical Risk Management Guidelines: A best practice guide [Internet]. Perth: Department of Health;2019 [cited 2021 Mar 15]. Available from URL: https://ww2.health.wa.gov.au/-/media/Files/Corporate/general-documents/Quality/PDF/WA-Health-Clinical-Risk-Management-Guidelines.pdf

Abrams and Greenhawt (2020) concluded that risk consist of the hazardous event and a public perception of that event and that risk communication can influence on that perception.

Monitor and review enable evaluation of the outcomes, so any issues can be identified and further improved (Figure 1.1).[18]

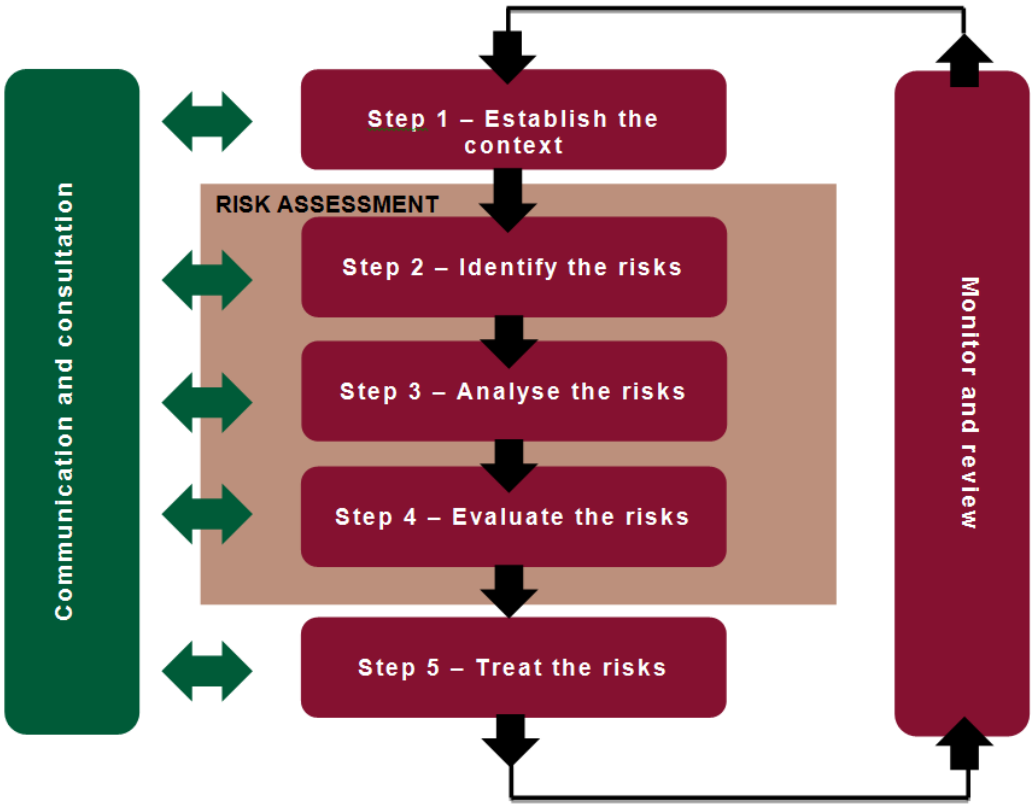

Figure 1.1: Risk management process

Adopted from: Government of Western Australia; Department of Health. Clinical Risk Management Guidelines: A best practice guide [Internet]. Perth: Department of Health;2019 [cited 2021 Mar 15]. Available from URL: https://ww2.health.wa.gov.au/-/media/Files/Corporate/general-documents/Quality/PDF/WA-Health-Clinical-Risk-Management-Guidelines.pdf

18. Government of Western Australia; Department of Health. Clinical Risk Management Guidelines: A best practice guide [Internet]. Perth: Department of Health;2019 [cited 2021 Mar 15]. Available from URL: https://ww2.health.wa.gov.au/-/media/Files/Corporate/general-documents/Quality/PDF/WA-Health-Clinical-Risk-Management-Guidelines.pdf

1.5 Reasons for Selecting Statins as a Case Scenario

Risk is associated with any drug treatment, including the treatment with statins. Careful assessment of risk versus benefits needs to be done so maximal effectiveness of statin treatment can be achieved.

The benefits of statins are documented in patients with hypercholesterolaemia and/or diabetes mellitus type 2. A meta-analysis by De Vries et al (2012) reports that when statins are used in patients with diabetes for primary prevention of ASCVD, there is significant reduction of first-time appearance of major cardiovascular or cerebrovascular events. Naeem et al (2018) supports this finding suggesting that when used for primary prevention in patients with diabetes, statins reduced cardiovascular events (Collins et al, 2003; Colhoun et al, 2004; Sever et al, 2005; Nakamura et al, 2006). A meta-analysis of 18 686 patients with diabetes (17 220 with diabetes mellitus type 2), of whom 63% did not have any previous cardiovascular event, showed that statins decreased 5-year incidence of stroke, major coronary and vascular events and requirement of coronary revascularisation (Kearney et al, 2008).

Therapy with statins reduced the risk of CVD related morbidity and mortality and all-cause mortality in patients with increased cardiovascular risk but without previous cardiovascular events. In this systematic review by Chou et al (2016) patients were at increased cardiovascular risk due to presence of diabetes mellitus type 2, dyslipidaemia, hypertension or some other risk factor or condition.

A meta-analysis by Tonelli et al (2011) included patients with 10-year cardiovascular risk <20%, without previous cardiovascular events and diabetes, with average LDL-C levels of 4.0 mmol/L (range 2.8-5.2 mmol/L). It was shown that statins in these patients prevent

death and cardiovascular morbidity. This finding is supported by a meta-analysis by Taylor et al (2013) which found that in patients with elevated blood cholesterol, but without prior cardiovascular events, treated with statins, all-cause mortality was decreased. Even in patients with 5-year risk lower than 10% and without history of any vascular events, diabetes or chronic kidney disease, the risk of major cardiovascular events is significantly reduced when LDL-C levels are decreased with statin (Mihaylova et al, 2012). Vallejo-Vaz et al (2017) performed analysis of WOSCOPS trial which included patients with elevated LDL-C ≥190 mg/dL (4.9 mmol/L) without any vascular disease at baseline. The effect of pravastatin on coronary heart disease and major adverse cardiovascular events was observed in 4.9 years of randomised trial and on mortality outcomes during 20 years of follow-up. All outcomes were significantly reduced by pravastatin during both 5 and 20 years of follow-up. Yusuf et al (2016) included men ≥55 and women ≥65 with intermediate CVD risk, and without any current CVD. Participants had baseline lipid levels within range. They were treated with rosuvastatin 10 mg for 5.6 years. These patients had significantly lower risk of CVD, when compared to placebo.

A meta-analysis by Mills et al (2008) concluded that statins, when used for primary prevention in diabetes mellitus type 2 and hypercholesterolaemia significantly reduced all-cause mortality. The meta-analysis by Mills et al (2011) included 170 255 patients who were taking statins both for primary and secondary prevention. It was shown that statins significantly reduce major CVD events and all-cause mortality. This finding is supported by Naci et al (2013) and their meta-analysis with 199 721 participants where it is shown that statins significantly reduced all-cause mortality and major coronary events when used both as primary and secondary prevention.

Baigent et al (2010) in their meta-analysis with more than 170 000 patients who took statin either for primary or for secondary prevention, concluded that with further

reductions in LDL-C, incidence of major vascular effects was lowered. Similar findings were published by Ridker et al (2016). They performed secondary analysis of JUPITER trial and showed that percentage LDL-C reduction was significantly correlated with the incidence event rate of ASCVD. As the percentage reduction of LDL-C was increasing, the ASCVD incidence was decreasing. The JUPITER trial enrolled asymptomatic patients, without previous ASCVD and diabetes, with LDL-C levels <130 mg/dL (3.4 mmol/L) and high-sensitivity C-reactive protein ≥2 mg/L. These findings are supported by a meta-analysis carried out by Silverman et al (2016), which reported that LDL-C levels are in a linear correlation with the rate of cardiovascular events.

Recommendation of guidelines[19] is that all patients with diabetes aged 40-75 without atherosclerotic disease, should be prescribed at least moderate-intensity statin (Arnett et al, 2019; Grundy et al, 2019; Cosentino et al, 2020). In patients aged 40-75 years and with hypercholesterolaemia without diabetes mellitus, 10-year CVD risk needs to be assessed and, accordingly, statins can be prescribed (Arnett et al, 2019; Grundy et al, 2019; Mach et al, 2020).

Low-intensity statins reduce LDL-C levels usually by <30%, moderate-intensity statins by 30% to 49% and high-intensity statins usually by ≥50% (Stone et al, 2014) (Table 1.1). There is individual variability in response to different statins, and this should be taken into consideration prior to prescribing and when there is a poor response to statin treatment (Karlson et al, 2016). There is evidence that lower doses of statins can be used in different Asian populations when compared to Caucasian with the same efficacy (Nakamura et al, 2006; Hu et al, 2013; Naito et al, 2017).

19. American Diabetes Association. Diabetes Care. Standards of medical care in diabetes – 2021 [Internet]. Arlington, VA: American Diabetes Association; 2021;44(1) [cited 2021 Mar 15]. Available from URL https://care.diabetesjournals.org/content/diacare/suppl/2020/12/09/44.Supplement_1.DC1/DC_44_S1_final_copyright_stamped.pdf

Table 1.1: Statin intensity based on the potential to reduce LDL-C levels

Statin	***Low-intensity*** **Reduction of LDL-C levels by <30%**	***Moderate-intensity*** **Reduction of LDL-C levels by 30% - 49%**	***High-intensity*** **Reduction of LDL-C levels by ≥50%**
Atorvastatin	N/A	10 mg to 20 mg	40 mg to 80 mg
Fluvastatin	20 mg to 40 mg	40 mg x 2/daily or XL 80 mg	N/A
Lovastatin	20 mg	40 mg to 80 mg	N/A
Pitavastatin	N/A	1 mg to 4 mg	N/A
Pravastatin	10 mg to 20 mg	40 mg to 80 mg	N/A
Rosuvastatin	N/A	5 mg to 10 mg	20 mg to 40 mg
Simvastatin	10 mg	20 mg to 40 mg	N/A

Adopted from: Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019;139:e1082-143.

1.6 Lacunae in Treatment with Statins

With strong evidence and clear recommendations for statin therapy, there are still treatment gaps for some specific groups of patients.

The National Committee for Quality Assurance issued a report where in 2018, among patients with diabetes mellitus type 2 in the USA, 61-74.4% were on statin treatment.[20] The data from 2016 showed that 58.9-70.7% of patients with diabetes mellitus type 2 were taking statin.[20]

20. National Committee for Quality Assurance (NCQA). Statin Therapy for Patients With Cardiovascular Disease and Diabetes (SPC/SPD) [Internet]. Washington: NCQA;2020 [cited 2021 Mar 15]. Available from URL: https://www.ncqa.org/hedis/measures/statin-therapy-for-patients-with-cardiovascular-disease-and-diabetes/

The data from the annual nationwide survey in the USA (Morbidity and Mortality Weekly Report) during the period of 2013-2014, statin use was 54.5% amongst patients who were eligible for cholesterol management. It was estimated that around 39.1 million eligible adults are not being prescribed statins for the management of their CVD risk (Wall et al, 2018). In a retrospective longitudinal study of 786 million USA patients during the period 2002-2013, it was reported that, during the study period of 12 years, statin use slowly increased from 33.4% to 52.7% in patients with diabetes and 28.1% to 47% in patients with hyperlipidaemia (Salami et al, 2017).

A study by Ueda et al (2018) aimed to examine statin use in USA and England and showed that 46% of high CVD risk patients in England are not using statins (28% of those have diabetes), while in USA 49.7% high risk CVD patients are not using statins (45.2% of those are with diabetes). Amongst patients with moderate CVD risk, in England 78.2% and in the USA 73% are not using statins. This means that, amongst patients with moderate to high CVD risk, in England 5.09 million patients are not using statins and in USA 25.5 million patients are not on statin treatment. If statins are given to those who are eligible for statin treatment, but are not using them, it was estimated that around 229 000 CVD events could be prevented in England and another 1 000 000 CVD events in USA, over a period of 10 years (Ueda et al, 2018).

A national retrospective cohort study analysed United Kingdom general practice and it included around 5 million patients in the period 2008-2010 (Wu et al, 2013). There were over 1 300 000 eligible patients without evidence of any past ASCVD and of those, 38.2% who were prescribed statins were eligible and 28% of those eligible were given statins (Wu et al, 2013).

Byrne et al (2018) reported that amongst patients with diabetes in Ireland, 57.8% were on statin therapy. For patients with hypercholesterolaemia, 44% were taking statins. Amongst Canadian patients with diabetes managed in the community, those with coronary artery disease (CAD) were better treated for cardiovascular risk factors. Patients with diabetes, but without CAD were less likely to be prescribed a statin (75.7% in comparison to 88.1% of patients with CAD who received statin) and had higher LDL-C levels (Grenier et al, 2016). A study from China showed that, amongst Chinese patients with diabetes, but without previous ASCVD, 85% were receiving a statin (Liu et al, 2019). A study by Urbonas et al (2020) enrolled patients from Lithuania who presented with diabetes, dyslipidaemia and/or hypertension and who were eligible for statin treatment for primary CVD prevention. The study showed that 52% of the patients with high CVD risk and 31% of those with very high CVD risk were using statins.

Bradley et al (2019) investigated the reasons why patients who are eligible to take a statin, were not on that treatment. Twenty-seven percent of the patients eligible for the statin, were not taking the drug. Among those, 59% have never been offered a statin, 31% discontinued the treatment and 10% refused statin. Amongst those who have never been offered a statin, 68% patients said they would use a statin and 60% of those who discontinued treatment on their own, would start using a statin again.

Pharmacist prescribing can help in filling the existing treatment gaps. Anderson et al (2020) showed that a pharmacist prescriber increased percent of the patients with diabetes mellitus type 2 who were taking statin from 65.7% at the beginning of the study, to 87.1%. This finding shows the importance of the pharmacists to extend the scope of practice to include prescribing.

1.7 Access to Healthcare Professionals

Lack of access to healthcare professionals can have consequences on patients' health. Khatib et al (2014) reported that lack of access to healthcare provider, available time and high workload for healthcare providers (of whom, 67% were physicians), were reported as some of the reasons of suboptimal blood pressure control. Report from Canada states that, in 2017 around 4.7 million people aged 12 years and older, did not have a regular healthcare provider (general practitioner, medical specialist or nurse practitioner).[21] As a solution, Khan et al (2019) calls for implementation of pharmacist prescribing in Canada for hypertension management in order to help medical practitioners' exhaustion.

Pharmacists are primary healthcare professionals, who are available and highly accessible to patients (Tsuyuki et al, 2018) and are in ideal position to fill in the treatment gap.

Older patients and those with existing CVD disease (Mc Namara et al, 2012) and with diabetes (Shiu et al, 2006; Mc Namara et al, 2012) visited community pharmacist more often than they visited general practitioner. Tsuyuki et al (2018) estimated that patients see their primary care pharmacist between 1.5 and 10 times more frequently than their primary care physician.

In Malta, the number of medical practitioners per capita steadily increased since 2009 and in 2017 was above EU average. [22]

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21. Statistics Canada. Health Fact Sheets: Primary health care providers, 2017 [Internet]. Ottawa: Statistics Canada; 2019 [cited 2021 Mar 15]. Available from URL: https://www150.statcan.gc.ca/n1/en/pub/82-625-x/2019001/article/00001-eng.pdf?st=PUZERCRQ
22. Azzopardi-Muscat N, Buttigieg S, Calleja N, Merkur S. Health Systems in Transition: Malta Health System Review [Internet]. Malta;2017;19(1):1-137 [cited 2021 Mar 15]. Available from URL: http://www.euro.who.int/__data/assets/pdf_file/0009/332883/Malta-Hit.pdf?ua=1

According to the Eurostat, in Malta in 2014, 40% of the population visited a GP during the previous four weeks before the survey.[23] In most EU Member States in 2018, average visit of GPs was between 4.4 and 10.0 per year.[23] In the Mediterranean Institute of Primary Care Patient Questionnaire 2009, nearly 90% of interviewed people in Malta, saw their GP in the previous year and people reported great accessibility of GPs in Malta. It was stated that expectations of GP service in Malta were high-quality services even out-of-hours and respondents reported that they wanted enough time per visit and that they do not like to be rushed. One of the suggestions for improvement of GP service was better accessibility, especially during out-of-hours. Most participants (80%) would like to visit one GP of their choice every time they are in need, rather than to change and visit different GPs.[24]

A report for Malta's Health System from 2019 stated that ageing private GPs as well as junior doctors who are hesitant to work in private solo practices, represent challenges who are changing private healthcare model and need to be addressed.[25] Pharmacist prescribers could be a solution to these challenges and could increase the access to healthcare especially out-of-hours.

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23. Eurostat. Statistics Explained. Healthcare activities statistics – consultations, 2018 [Internet]. Luxembourg: Eurostat; 2020 [cited 2021 Mar 15]. Available from URL: https://ec.europa.eu/eurostat/statistics-explained/index.php/Healthcare_activities_statistics_-_consultations#Consultations_of_doctors

24. Soler JK, Borg M, Stabile I, Mifsud A, Abela G, Farrugia D. Mediterranean Institute of Primary Care Patient Questionnaire 2009. Malta; 2009 [cited 2021 Mar 15]. Available from URL: http://www.mipc.org.mt/documents/MIPC%20Patient%20Questionnaire%20report.pdf

25. Organisation for Economic Co-operation and Development (OECD). Malta: Country Health Profile 2019, State of Health In the EU [Internet]. Paris: OECD; 2019 [cited 2021 Mar 15]. Available from URL: https://www.oecd-ilibrary.org/docserver/05db1284-en.pdf?expires=1606919236&id=id&accname=guest&checksum=81B347FCE9573B9E06125F8B958CF7E5

1.8 Statin Prescribing Protocols in Malta

The Government Formulary List (GFL) in Malta consists of two lists: Hospital Formulary List and Out-Patients Formulary List. The Out-Patients Formulary List is intended to be used by government pharmacies and by the Pharmacy Of Your Choice (POYC) scheme.[26] POYC is a national pharmaceutical service which provides eligible patients free pharmaceutical devices and medicines, listed on the Out-Patients Formulary List.[27]

Three statins can be found on both Hospital Formulary List and Out-Patients Formulary List: atorvastatin (10 mg, 20 mg and 40 mg), rosuvastatin (20 mg and 40 mg) and simvastatin (10 mg, 20 mg and 40 mg).[28,29] Fluvastatin has been removed from the GFL in 2018.[30] By the same protocol[30] atorvastatin became first-line statin treatment. Atorvastatin and simvastatin can be used as a first-line statin treatment, while rosuvastatin can be prescribed only when target level of LDL-C has not been achieved (low to moderate risk: LDL-C≤3mmol/L; high risk LDL-C≤1.8mmol/L) with maximum dose of atorvastatin for a period of minimum 3 months.[30]

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30. Office of the Deputy Prime Minister, Ministry for Health. Deletion of Fluvastatin and Changes in Statin Entitlement [Internet]. Valletta: Office of the Deputy Prime Minister, Ministry for Health; 2018 [cited 2021 Mar 15]. Available from URL: https://deputyprimeminister.gov.mt/en/pharmaceutical/Documents/Circulars/2018/circular_54_2018.pdf

1.9 Rationale of the Study

Studies regarding pharmacist prescribing in Malta have been undertaken (Tabone et al, 2013; Vella et al, 2014; Vella et al, 2015; Attard Pizzuto, 2016; Aquilina et al, 2018; Micallef, 2019), but to the best knowledge of the investigator, there is no research which assesses pharmacist prescribing, from a pharmacist and medical practitioner perspective, of low- and moderate-intensity statins to patients with hypercholesterolaemia and/or diabetes mellitus type 2 without previous ASCVD.

This research assesses the risk associated with pharmacist prescribing. By identifying the potential risks, both pharmacists and medical practitioners, can reduce the risks and make the statin treatment safer for the patient. This research offers suggestions that could potentially reduce the risks associated with prescribing of statins and factors that could ease the process of implementation of pharmacists prescribing in Malta.

1.10 Aim and Objectives

Aim was to determine the risks related to prescribing low- and moderate-intensity statins, both by medical practitioners and pharmacists.

Aim was achieved by:

i) Developing and validating two questionnaires, one for medical practitioners and one for pharmacists, to assess their perceptions regarding the risks associated with prescribing of statins for primary prevention.

ii) Developing a regression model to statistically analyse and identify differences, if any, of risks involved when statins are prescribed by medical practitioners and by pharmacists.

Chapter 2

Methodology

2.1 Research Design

This cross-sectional study assessed the attitudes and opinions related to prescribing of statins for primary CVD prevention using questionnaires. Medical practitioners and pharmacists were asked to rate the risks associated with prescribing of statins by medical practitioners and pharmacists. Medical practitioners and pharmacists rated the importance of factors which could potentially ease the implementation of pharmacist prescribing in Malta.

2.1.1 Questionnaire Development

Two questionnaires, one for medical practitioners and one for pharmacists, were developed and titled 'Statin Prescribing Questionnaire for Medical Practitioners' (SPQ_{MedPr}) and 'Statin Prescribing Questionnaire for Pharmacists' (SPQ_{Pharm}) respectively (Appendix 1). Questions were adapted from Krempf et al (2015), Attard Pizzuto (2016) and Courtenay et al (2018) and developed by the principal investigator for the purpose of this research.

Questions were developed using 5-point Likert scale of 1 to 5 where 1 was the lowest score and 5 was the highest score. The other types of the questions used were single-answer multiple-choice questions and dichotomous closed-ended questions.

Both questionnaires consisted of two parts. Part ONE had four sections with 21 questions. Part TWO consisted of one question. Sections were: *Demographics (Section I), Statin prescribing (by Medical Practitioners) (Section II), Statin Prescribing by Pharmacists (Section III)* and *Medical practitioner–Pharmacist Collaboration (Section IV).*

Part ONE

Section I: Demographics

This section included four questions, all of which were single-answer multiple-choice questions. The questions asked participants for the years of professional experience, level of postgraduate training (for medical practitioners) or place of work (for pharmacists), most common patient age group that participants come into contact with and the average number of patients with hypercholesterolaemia and/or diabetes mellitus type 2 that participants encounter during their practice.

Section II: Statin prescribing (by Medical Practitioners)

This section consisted of eight questions of which six made use of a 5-point Likert scale ranging from 1 to 5 and two were single-answer multiple-choice questions.

In the SPQ_{MedPr} this section was named *Statin prescribing by Medical Practitioners*. Medical practitioners were asked what drug- and patient-related information as well as other factors, influence prescription of statins. Two single-answer multiple-choice questions assessed practices of lipid monitoring and liver function monitoring in patients taking statins. In this section, risks associated with statin prescribing by medical practitioners were assessed. The last question in this section examined awareness of guideline recommendations regarding indications for statin prescribing, monitoring requirements, interactions, side-effects and contraindications of statin treatment.

In $SPQ_{Pharm,}$ section II was named *Statin prescribing*. The number of questions and their structure was the same as in SPQ_{MedPr}. The difference in the title was made because while for medical practitioners their own practices regarding statin prescribing were assessed, for pharmacists, their awareness of recommendations for statin prescribing was assessed.

Section III: Statin Prescribing by Pharmacists

The potential scenario of pharmacist prescribing of statins was assessed in this section. Pharmacists would prescribe low- and moderate-intensity statins to patients aged 40-75 years with hypercholesterolaemia and/or diabetes mellitus type 2 for primary prevention of ASCVD, by following predefined inclusion and exclusion criteria. Low- and moderate-intensity statins were chosen because they are associated with less side-effects when compared to high-potency statins (Ran et al, 2017; Lee et al, 2018; Thongtang et al, 2020). Patients would either present their laboratory results with elevated cholesterol levels or would have a diagnosis of diabetes mellitus type 2. If the pharmacist could not confirm the patient's diagnosis, the signs and/or symptoms were severe, or if pharmacists had any uncertainty, the pharmacist would refer the patient to a medical practitioner.

This section had five questions of which four were using 5-point Likert scale of 1 to 5 and one was dichotomous closed-ended question.

Questions regarding pharmacists' competence for prescribing of statins, risks associated with pharmacist prescribing of statins, the reasons why pharmacists should not be given prescribing rights as well as how this new scenario would affect medical practitioners, were asked. As for the closed-ended question, participants were asked whether pharmacists in Malta should be given statin prescribing rights.

Section IV: Medical practitioner–Pharmacist Collaboration

There were four questions in this section of which two made use of a 5-point Likert scale of 1 to 5 and two were dichotomous closed-ended questions.

In this section, the opinion regarding benefits of medical practitioner-pharmacist collaboration was estimated. The aspects that healthcare professionals collaborated on

were also assessed. With closed-ended questions, participants were asked whether they collaborate with the pharmacist/medical practitioner in their daily practice and if there was no collaboration, whether they were willing to start.

Part TWO

Both medical practitioners and pharmacists rated the importance of fourteen factors which could potentially ease the implementation of pharmacist prescribing in Malta, using a rating scale of 1 to 5 (where 1 was not important at all and 5 was very important).

All questions had a comment section underneath where respondents could write additional thoughts and opinions.

2.1.2 Questionnaire Validation

After questionnaires development, the content validity of the questionnaires was examined using a two-round modified Delphi method. While assessing content validity, both qualitative and quantitative analyses were performed. Qualitative analysis implied adding missing items which should be mentioned as new options or rewording of existing questions due to grammar inaccuracies and insufficient clarity, based on the recommendations of panel members. As part of quantitative analysis, experts rated relevance of the questions and based on the relevance rating scores, questions were removed or retained in the questionnaires.

An expert panel of six members was used, consisting of three medical practitioners (one vascular surgeon, one cardiologist and one general practitioner) and three pharmacists (one academic, one hospital and one community pharmacist). Gender was equally

distributed. Experts were selected on the basis of personal contact and representativeness was not achieved. Experts were contacted either physically or via email and all agreed to participate. A statistician was also consulted to approve scales and scoring systems.

Round I of validation

Upon accepting to participate, panel members were contacted via email. A covering letter explaining the purpose of the study and instructions for questionnaire validation were sent. A reminder was sent to those panel members who did not send validated questionnaires after 10 days.

During validation, panel members could comment what they would like to change with respect to presentation, clarity or content of the questions. Panel members rated the relevance of the questions, where option 1 was 'not relevant' and option 5 was 'highly relevant'. The structure of the questions was assessed and any other options that could be added were suggested.

For the qualitative analysis, recommendations were accepted either if three out of the six members put forward the same suggestion, and/or if the recommendation was evidence-based. When the first round of validation was completed, changes were made based on recommendations.

For the quantitative analysis both item-level content validity index (I-CVI) and scale-level content validity index (S-CVI) were calculated. I-CVI was calculated as the proportion of the experts who rated the question 'relevant', with 4 or 5 on the 5-point Likert scale.

For the assessment of S-CVI, the following two methods were used:

- S-CVI universal agreement (S-CVI/UA), for which the proportion of the questions that achieved relevance rating of 4 or 5 by all the experts was used.
- S-CVI average (S-CVI/Ave), where the average value of all the I-CVIs was used.

I-CVI helps with the decision to omit, revise or keep an item (Almanasreh et al, 2019). In order to have excellent content validity, the minimal recommended values for CVIs were: I-CVI of at least 0.78 (Polit and Beck, 2006; Polit et al, 2007; Sangoseni et al, 2013; Vrbnjak et al, 2017), S-CVI/Ave of minimum 0.90 (Polit and Beck, 2006; Pierce et al, 2016; Chiwaridzo et al, 2017; Vrbnjak et al, 2017; Lam et al, 2018) and S-CVI/UA of minimum 0.80 (Polit et al, 2007).

After both qualitative and quantitative analyses were performed, questionnaires were ready for the second validation round.

Round II of validation

The same expert panel was contacted after three weeks for the second round of validation and all the members agreed to participate. The questionnaires were sent via email and a reminder was sent after eight days. After receiving all the questionnaires in the second round of validation, both qualitative and quantitative analyses were performed. After implementing the recommended changes and comparing the results from both rounds of the validation, the questionnaires were then tested for reliability.

2.1.3 Test-retest Reliability

To determine test-retest reliability of the questionnaires (stability of the questionnaire during time), seventeen pharmacists were recruited. They were selected through personal contact; therefore representativeness was not achieved. All of the pharmacists were asked in person whether they would like to participate in reliability testing and all agreed. Questionnaires were given to them either in person or were sent via email. Questionnaires were anonymous. Participants were asked to mark the questionnaire, using a symbol or any word for traceability purposes. All seventeen pharmacists completed the questionnaires. Seven days after collection of completed questionnaires, the same questionnaire was given to each pharmacist to be filled in again. Participants needed to mark the questionnaire using the same symbol or word which they were using for the first time. Fifteen pharmacists (88.2%) completed the questionnaire for the second time.

For the analysis of the answers, IBM SPSS Statistics Version 25.0 was used. When responses had a nominal scale, Kappa test was used and for those with ordinal scale, Kendall-Tau test was applied. For both Kappa and Kendall-Tau test, the null hypothesis specified that test-retest reliability was poor and was accepted if p value exceeded 0.05 level of significance. The alternative hypothesis specified that test-retest was satisfactory and was accepted if p value was less than 0.05.

Spearman correlation test was also conducted, analysing the relationship between two answers for each individual question and for all the questions at once. The normality assumption was not tested since most of the variables were rated using a Likert scale of 1 to 5, which is ordinal categorical scale, and the non-parametric test, Spearman correlation test was chosen. The null hypothesis stated that there was no relationship between two answers and that stability during time of specific individual question or of

the whole questionnaire was poor. The alternative hypothesis specified that there was a significant relationship between the two answers and that stability during time was satisfactory, for specific individual question or for the whole questionnaire. If p-value was less than 0.05, relationship between two answers was statistically significant and thus not attributed to chance.

2.1.4 Ethics Approval

Ethics approval was sought and obtained from the Faculty Research Ethics Committee (FREC) (Appendix 2).

2.2 Sampling

The estimated number of registered pharmacists in Malta at the time of study was 1250 and the number of medical practitioners who belong to either the family medicine or general/internal medicine specialty was 531.[31] These specialities were chosen because although all medical practitioners can prescribe statins, these specialities are easily accessible for the patients, both in public and in private sector and serve as 'gatekeepers' for different health services.[22]

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22. Azzopardi-Muscat N, Buttigieg S, Calleja N, Merkur S. Health Systems in Transition: Malta Health System Review [Internet]. Malta;2017;19(1):1-137 [cited 2021 Mar 15]. Available from URL: http://www.euro.who.int/__data/assets/pdf_file/0009/332883/Malta-Hit.pdf?ua=1

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2.2.1 Research Setting

The principal investigator visited community pharmacies and private clinics where medical practitioners with specialities of family medicine or general/internal medicine attend.

2.3 Data Collection

Questionnaires were distributed both electronically and in person by the principal investigator, to medical practitioners and pharmacists. For electronic distribution, online versions of the questionnaires were developed using Google Docs.
For electronic distribution to medical practitioners, the following organisations were contacted: Malta College of Family Doctors (174 full members and 3 associate members), where questionnaire was send twice, The Association of Private Family Doctors (98 members), questionnaire was sent once and Primary HealthCare Malta, questionnaire was sent once.

For pharmacists, the questionnaire was distributed via social media, in a closed group having 885 members including students who were not eligible to participate. The questionnaire was also sent once by the Department of Pharmacy to alumni members (180 pharmacists).

Questionnaires were also distributed in person to 170 pharmacists working in community pharmacies and 60 medical practitioners working in clinics in community pharmacies. To avoid duplication of the results, all pharmacists and medical practitioners who were

visited were told in person that if they already responded to the questionnaire online, they do not need to fill in the physical questionnaire again and vice-versa. Participants were chosen using the convenience sample method.

Questionnaires were anonymous and self-administered. In order to provide complete anonymity of participants, the principal investigator had a sealed box with an opening on top where participants could put their completed questionnaire. Participation was voluntary. The questionnaire took 10 to 15 minutes to complete.

2.4 Data Analysis

For the analysis of the data, IBM SPSS Statistics Versions 27.0 was used. In order to analyse differences among mean rating scores of several related options, within one multiple-choice question, the Friedman test was used. Results were further supported with error bar graphs.

The Kruskal Wallis test was used to compare mean rating scores between different independent groups clustered by years of medical practitioners'/pharmacists' experience or clustered by information whether there was collaboration between different healthcare professionals. The Chi-Square test was used to compare two categorical variables.

For all the tests used, the null hypothesis stated that there was no statistically significant difference amongst groups and was accepted if p-value was more than 0.05, while the alternative hypothesis stated that there was statistically significant difference amongst groups and was accepted if p-value was less than 0.05.

Using the risk factors rated by participants while assessing the risk associated with statin prescribing, cluster analysis of all 13 risks factors was done. TwoStep clustering was used to indicate the optimal number of clusters and final clustering was performed using K-means.

A regression model I was developed to statistically analyse and identify differences, if any, of risks involved when statins are prescribed by medical practitioners and by pharmacists. The ANCOVA regression model was used. The dependant variable was 'Total risk' that was calculated as an average value of all thirteen (13) risk factors associated with prescribing, estimated by one healthcare professional. Each healthcare professional provided two answers, one for estimated risks associated with statin prescribing by medical practitioners, the other one for estimated risks associated with pharmacist prescribing of statins. All of the responses were included in the development of the final model.

Regression analysis ANCOVA was also used to estimate the relationship between predictors and the dependant variable (regression model II). The dependant variable was 'Total risk' and the predictors were: healthcare professional (medical practitioner or pharmacist) who estimated the risks by completing the questionnaire, years of healthcare professional's professional experience, the number of patients with hypercholesterolaemia and diabetes mellitus type 2 who healthcare professional encounters on weekly basis, attitude towards giving statin prescribing rights to pharmacists and whether there is routine collaboration with other healthcare professionals (medical practitioner or pharmacist). All responses were included in the final analysis.

For both regression model I and regression model II, all ANCOVA assumptions were tested and satisfied. Studentized deleted residuals were used for detection of outliers, which can interfere with the final models.

2.5 Protocols for Prescribing of Statins

Protocols for pharmacist prescribing of low- and moderate-intensity statins to patients with hypercholesterolaemia and/or diabetes mellitus type 2 without previous ASCVD were developed, following questionnaire results analysis, aiming at reducing the risks associated with statin prescribing (Appendix 3).

Chapter 3

Results

Content validity and test-retest reliability were assessed, for both of the questionnaires. After collection of SPQ_{MedPr} and SPQ_{Pharm}, final analysis of data was performed. Results from SPQ_{MedPr} and SPQ_{Pharm} are presented.

3.1 Content Validity

I-CVI and S-CVI were calculated for both SPQ_{MedPr} and $SPQ_{Pharm,}$ for both rounds of modified Delphi method (Table 3.1).

Table 3.1: CVI values of questionnaires in both rounds of modified Delphi method

	SPQ_{MedPr}		**SPQ_{Pham}**	
	Round I	Round II	Round I	Round II
I-CVIs	0.83-1	1	0.83-1	1
S-CVI/UA	0.82	1	0.90	1
S-CVI/Ave	0.97	1	0.98	1

In both rounds, for both questionnaires, the CVI values demonstrated excellent agreement among experts and acceptable content validity. None of the questions were removed from the SPQ_{MedPr} and SPQ_{Pharm}.

3.1 Test-retest Reliability

For each individual option, within every question, Kendall-Tau or Kappa test were done. Additionally, for every question, Spearman's correlation test was performed.

In the test questions, there was satisfactory test-retest reliability with p value less than 0.05. In 18 question options (from total 122) Kappa/Kendal-Tau test did not yield a p value because there was no or very little variation in responses.

In all of the questions, Spearman's correlation coefficient was above 0.7 ($p<0.001$ – 0.003) and for the whole questionnaire was 0.840 ($p<0.001$), which suggested satisfactory correlation and good test-retest reliability.

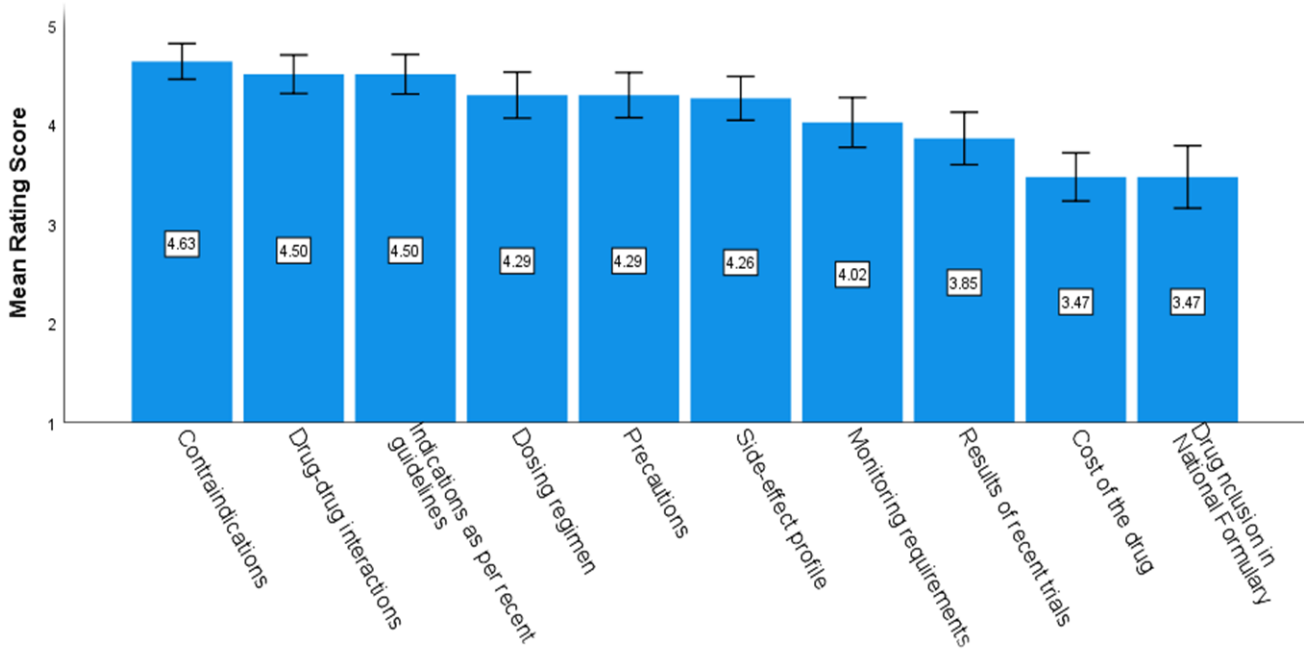
3.2 Analysis of SPQ_{MedPr}

Sixty-four medical practitioners answered the SPQ_{MedPr}. Thirty-two questionnaires were collected during personal visits (response rate 53.3%) and 32 were done online. In the final analysis 62 questionnaires were included since two questionnaires were incomplete.

The majority of medical practitioners had >20 years of medical experience (n=44, 71%), 11 (17.7%) had between 11-20 years of experience while 7 (11.3%) had 10 or less years of experience. Fifty-eight medical practitioners (93.5%) were specialists in family medicine, 3 were basic specialist trainee (4.8%) in family medicine, while one (1.6%) was a foundation doctor.

The age of the population commonly treated was the 19-65 range (n=54, 87.1%), while 8 medical practitioners (12.9%) were mostly treating the population aged more than 65 years. When asked what is the average number of patients with diabetes mellitus type 2 and hypercholesterolaemia they encounter per week, 32 medical practitioners (51.6%) replied '10-30' for patients with diabetes mellitus type 2 and 33 (53.2%) said '10-30' for the patients with hypercholesterolaemia. Nineteen medical practitioners (30.6%) have been seeing '<10' patients with diabetes mellitus type 2 per week and 14 (22.6%) have been seeing '<10' patients with hypercholesterolaemia per week.

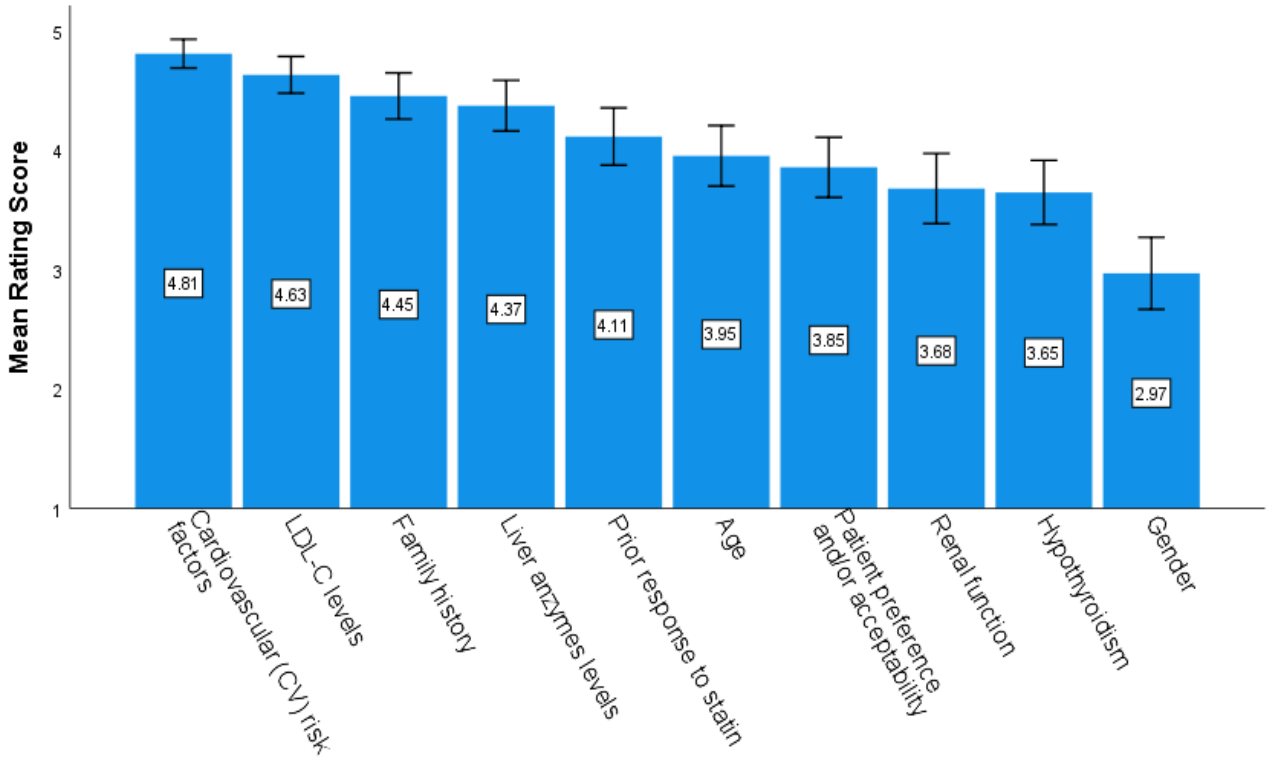
In order to evaluate medical practitioners' prescribing practices, the percentage of medical practitioners who chose the highest rating score (5) on the Likert scale was assessed. When medical practitioners were asked to rate the importance of drug-related information when prescribing statins, 44 (71%) said that 'contraindications' are very important. This was followed by 39 medical practitioners (62.9%) who replied that 'indications as per recent guidelines' are very important, while 38 (61.3%) rated 'drug-drug interactions' as very important. Thirty-three medical practitioners (53.2%) rated 'precautions' and 'dosing regimen' as very important drug-related information. Figure 3.1 represents the mean rating scores for the importance of drug-related information when prescribing statins for primary prevention of ASCVD in patients with hypercholesterolaemia and/or diabetes mellitus type 2. The highest mean rating score of 4.63 (out of 5) was assigned to 'contraindications' while the lowest mean rating score (3.47) was assigned to 'drug inclusion in National Formulary'. The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating scores of different answers.



$X^2(9) = 135.014$, $p<0.001$

Figure 3.1: Medical practitioners' mean rating scores when rating the importance of drug-related information when prescribing statins (N=62)

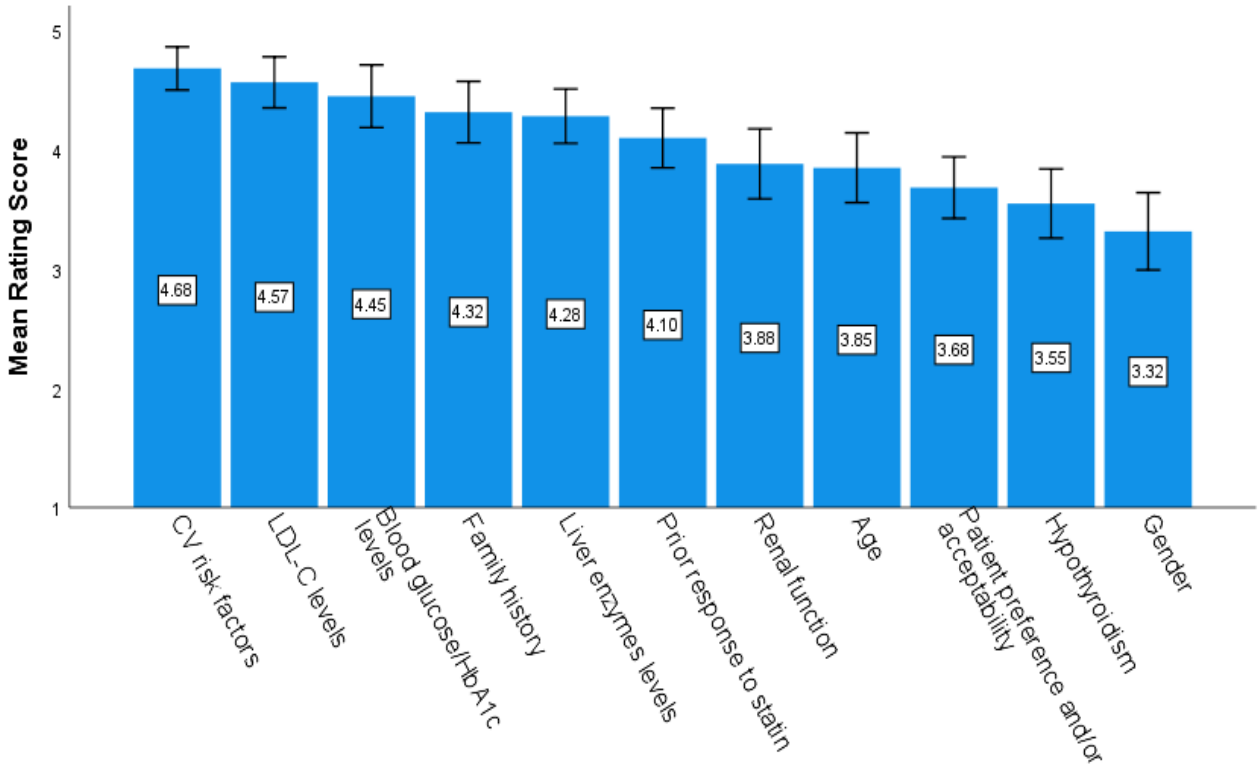
When asked about the importance of patient-related information that needed to be assessed when prescribing statins for patients with hypercholesterolaemia, 52 medical practitioners (83.9%) rated 'cardiovascular (CV) risk factors' as very important. This was followed by 'LDL-C levels' (n=43, 69.4%), 'family history' (n=36, 58.1%), 'liver enzyme levels' (n=34, 54.8%) and 'prior response to statin' (n=25, 40.3%). Figure 3.2 represents the mean rating scores regarding importance of patient-related information while prescribing statins for patients with hypercholesterolaemia, without previous ASCVD. The highest mean rating score (4.81) was assigned to 'cardiovascular (CV) risk factors' and the lowest mean rating score (2.97) was assigned to 'gender'. The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating scores of different answers.



$X^2(9) = 179.710$, $p<0.001$

Figure 3.2: Medical practitioners' mean rating scores when rating the importance of the patient-related information while prescribing statins for patients with hypercholesterolaemia without previous ASCVD (N=62)

When asked to rate the importance of patient-related information when prescribing statins for patients with diabetes mellitus type 2 without previous ASCVD, 48 medical practitioners (77.4%) rated 'CV risk factors' as very important. This was followed by 'LDL-C levels' (n=45, 72.6%), 'blood glucose/HbA1c levels' (n=45, 72.6%), 'family history' (n=36, 58.1%) and 'liver enzymes levels' (n=31, 50%). When assessing the mean rating scores (Figure 3.3) it was observed that the highest mean rating score (4.68) was assigned to 'CV risk factors' and the lowest rating score (3.32) was assigned to 'gender'. The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating scores of different answers.



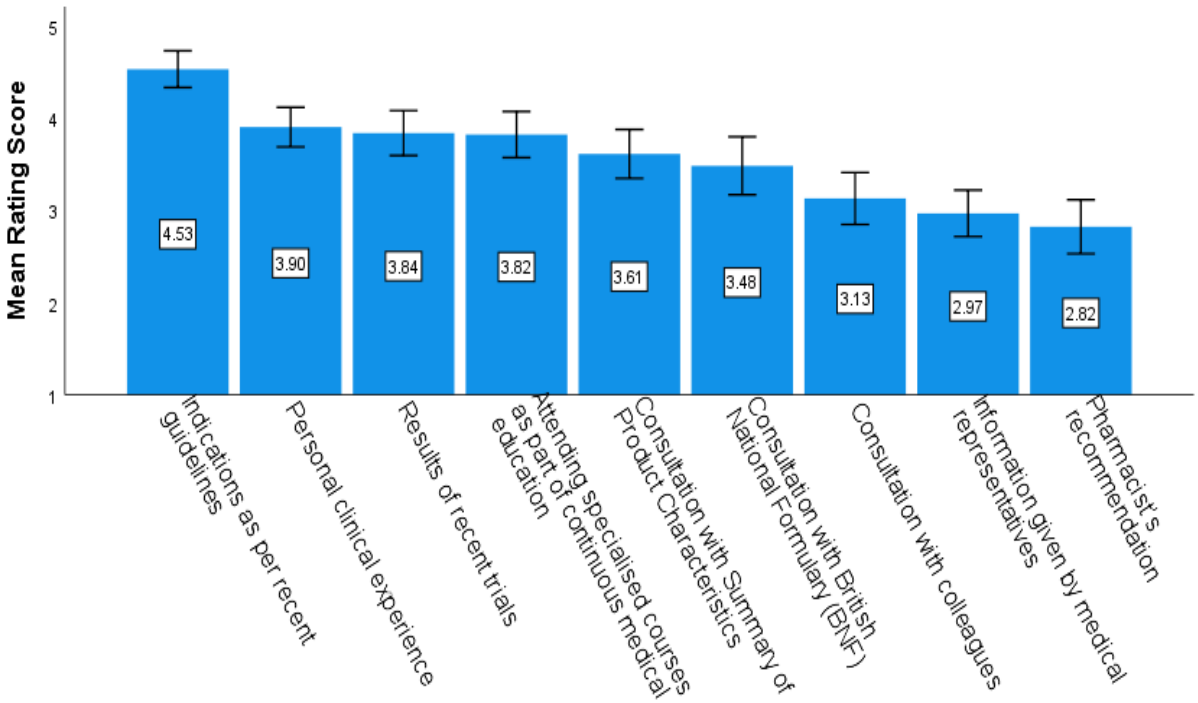
$X^2(10) = 145.575$, $p<0.001$

Figure 3.3: Medical practitioners' mean rating scores when rating the importance of the patient-related information when prescribing statins for patients with diabetes mellitus type 2 without previous ASCVD (N=62)

When medical practitioners were asked about monitoring habits of patients' lipid-profile when prescribing statins for patients with hypercholesterolaemia without previous ASCVD, 31 medical practitioners (50%) answered 'every 6 months', 15 (24.2%) 'yearly' and 6 (9.7%) 'every 3 months'.

When asked about monitoring of patients' liver function while prescribing statins for patients with hypercholesterolaemia and/or diabetes mellitus type 2 without previous ASCVD, 37 medical practitioners (59.7%) chose 'every 6 months', 7 (11.3%) medical practitioners answered 'yearly' and 7 (11.3%) chose 'every 3 months'.

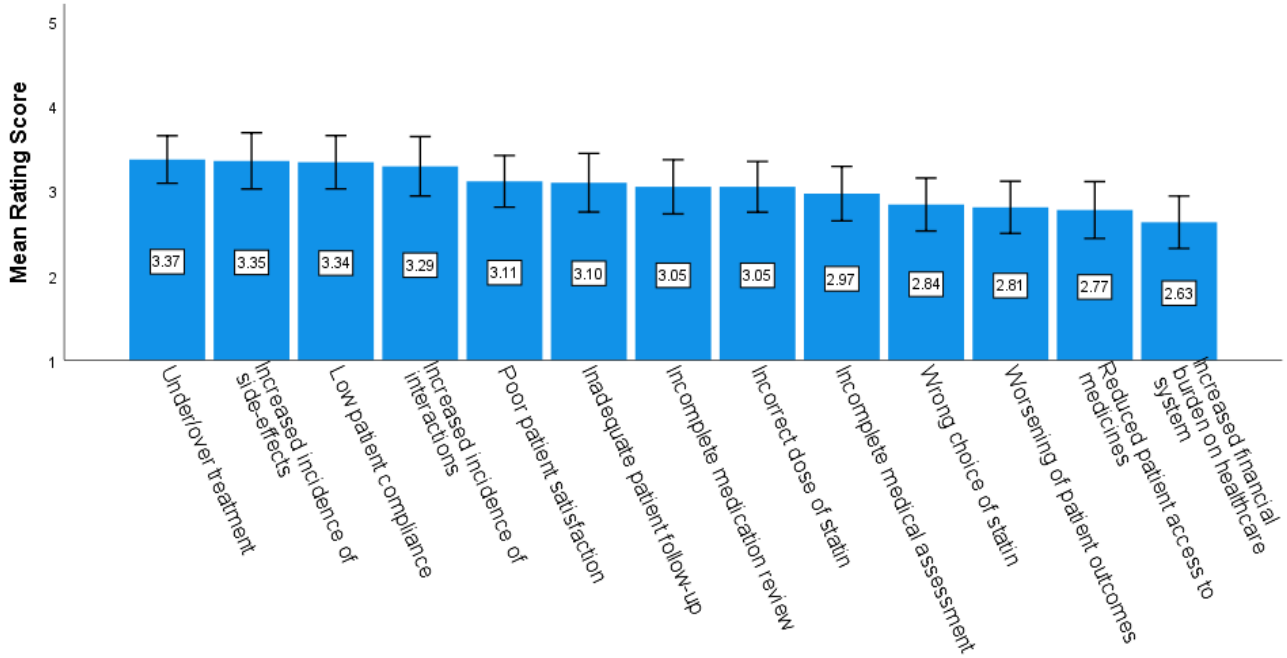
When assessing the importance of the factors that could influence the prescribing of statins 41 medical practitioners (66.1%) rated 'indications as per recent guidelines' as very important. This was followed by 'results of recent trials' (n=19, 30.6%), 'attending specialised courses as part of continuous medical education' and 'personal clinical experience' both at 25.8% (n=16) and 'consultation with British National Formulary (BNF)' and 'consultation with Summary of Product Characteristics' both at 24.2% (n=15). Figure 3.4 represents the mean rating scores regarding importance of the following factors that could influence prescribing of statins. The highest mean rating score (4.53) was given to 'indications as per recent guidelines' and the lowest (2.82) to 'pharmacist's recommendation'. The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating scores of different answers.



$X^2(8) = 152.357$, $p<0.001$

Figure 3.4: Medical practitioners' mean rating scores when rating the importance of the factors that could influence the prescribing of statins (N=62)

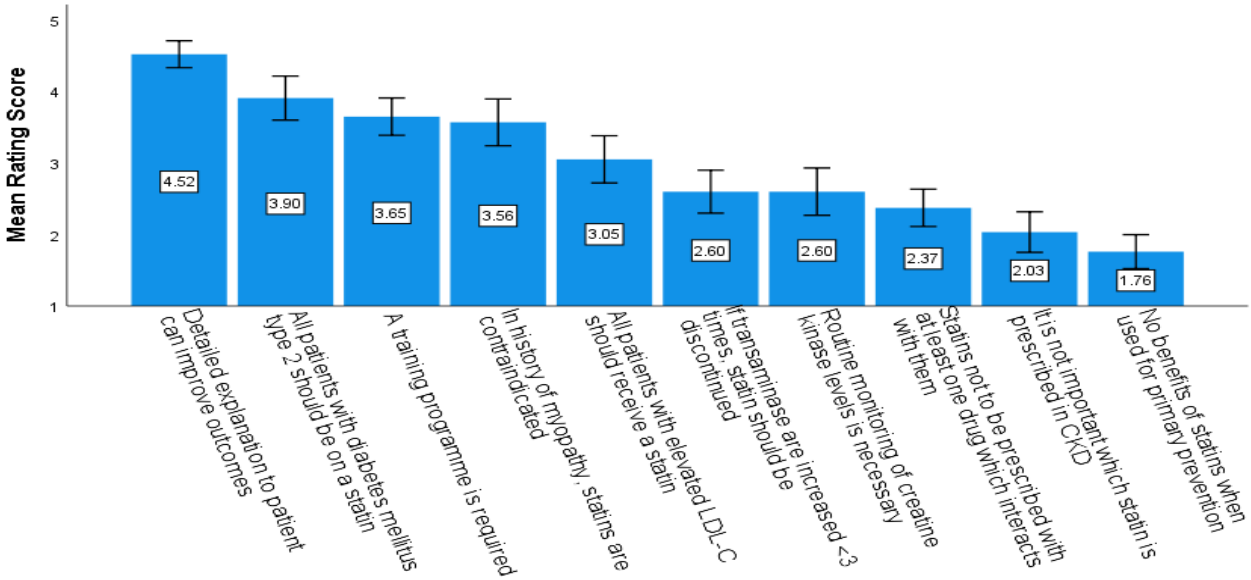
When asked what are the perceived risks associated with prescribing of statins by medical practitioners (where 1 was low risk and 5 was high risk), 15 medical practitioners (24.2%) thought that there is a high risk for the 'increased incidence of interactions'. Fourteen medical practitioners (22.6%) thought 'increased incidence of side-effects' was associated with a high risk, while 12 (19.4%) indicated 'low patient compliance' as high risk. This was followed by 'inadequate patient follow-up' (n=10, 16.1%) and 'under/over treatment' and 'poor patient satisfaction' both at 14.5% (n=9). Figure 3.5 represents the mean rating risk scores associated with prescribing of statins by medical practitioners. Medical practitioners thought that 'under/over treatment' represents the highest risk (3.37), while 'increased financial burden on healthcare system' represents the lowest risk (2.63). The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating risk scores of different answers.



$X^2(12) = 58.395$, $p<0.001$

Figure 3.5: Medical practitioners' mean rating scores when assessing the risks associated with prescribing of statins by medical practitioners (N=62)

Medical practitioners were asked to rate their level of agreement with specific statements regarding statin treatment, using scale of 1 to 5 where 1 was 'strongly disagree' and 5 'strongly agree'. Thirty-nine medical practitioners (62.9%) strongly agreed that 'detailed explanation to patient why statin is prescribed can improve outcomes', while 24 medical practitioners (38.7%) strongly agreed with the statement 'all patients with diabetes mellitus type 2, aged 40-75 years should be on a statin regardless of their LDL-C levels'. Figure 3.6 represents the mean rating scores of agreement regarding different statements related to statin prescribing. The highest level of agreement (4.52) was with the statement 'detailed explanation to patient why statin is prescribed can improve outcomes', while the lowest level of agreement (1.76) was related to 'there is a lack of beneficial effect of statins when used for primary prevention in patients aged 40-75 years with hypercholesterolaemia and/or diabetes mellitus type 2'. The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating scores of different answers.



$X^2(9) = 232.995$, $p<0.001$

Figure 3.6: Medical practitioners' mean rating scores representing the level of agreement with different statements regarding prescribing of statins (N=62)

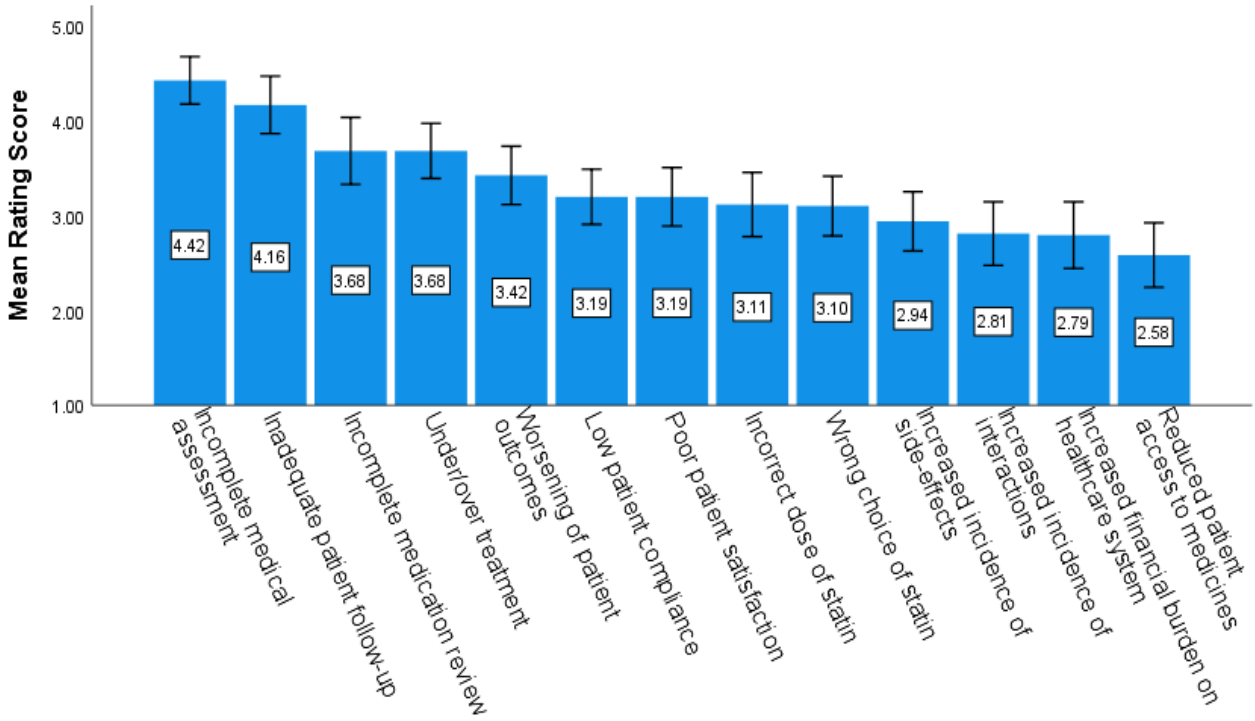
Table 3.2 represents the number of medical practitioners who disagreed, had neutral opinion or agreed with different statements related to prescribing of statins.

Table 3.2: The number of medical practitioners who agreed, had neutral opinion or disagreed with specific statements regarding prescribing of statins (N=62)

	Disagreement **Values 1 and 2** **n (%)**	**Neutral opinion** **Value 3** **n (%)**	**Agreement** **Values 4 and 5** **n (%)**
All patients with diabetes mellitus type 2, aged 40-75 years should be on a statin regardless of their LDL-C levels	10 (16.1)	6 (9.7)	46 (74.2)
All patients with elevated LDL-C, aged 40-75 years should receive a statin, regardless of their CVD risk	23 (37.1)	16 (25.8)	23 (37.1)
It is not important which statin is prescribed to patients with chronic kidney disease (CKD)	42 (67.7)	12 (19.4)	8 (12.9)
If transaminase levels are increased less than three times the upper limit of normal, statin should be discontinued	35 (56.4)	12 (19.4)	15 (24.2)
Routine monitoring of creatinine kinase levels (as a sign of myopathy) is necessary even in asymptomatic patients	36 (58.1)	9 (14.5)	17 (27.4)
In patients with history of myopathy, statins are contraindicated	15 (24.2)	13 (21)	34 (54.8)
There is a lack of beneficial effect of statins when used for primary prevention in patients aged 40-75 years with hypercholesterolaemia and/or diabetes mellitus type 2	53 (85.5)	6 (9.7)	3 (4.8)
Statins should not be prescribed to patients who have at least one drug which interacts with statins (example, amlodipine)	37 (59.7)	18 (29)	7 (11.3)
Detailed explanation to patient why statin is prescribed, can improve outcomes	2 (3.2)	3 (4.8)	57 (92)
An educational training programme on prescribing of statins is required	9 (14.5)	17 (27.4)	36 (58.1)

When asked whether pharmacists are competent to prescribe statins, on the scale of 1 (not competent at all) to 5 (highly competent), 17 medical practitioners (27.4%) thought that pharmacists are competent to prescribe statins (values 4 and 5 on Likert scale). Of those, 11 medical practitioners (17.7%) chose the value of 4 and 6 (9.7%) rated the pharmacists' ability to prescribe as highly competent (5). Twenty-two medical practitioners (35.5%) had a neutral opinion, while 23 medical practitioners (37.1%) thought that pharmacist are not competent. Of those, 8 medical practitioners (12.9%) assigned the value of 1 to pharmacist competence and 15 medical practitioners (24.2%) assigned the value of 2. The mean rating score of pharmacists' competence to prescribe statins for primary prevention to selected group of patients was 2.87, when rated by medical practitioners.

Medical practitioners were asked to estimate the risks associated with potential pharmacist prescribing of statins. Thirty-nine medical practitioners (62.9%) thought that 'incomplete medical assessment' presented the high risk for potential pharmacist prescribing, while 36 (58.1%) thought that 'inadequate patient follow-up' was associated with high risk. This was followed by 'incomplete medication review' (n=24, 38.7%), 'under/over treatment' (n=18, 29%) and 'worsening of patient outcomes' (n=14, 22.6%). Figure 3.7 represents the mean rating scores when assessing the risks associated with prescribing of statins by pharmacists. Medical practitioners thought that 'incomplete medical assessment' represents the highest risk (4.42), while 'reduced patient access to medicines' represents the lowest risk (2.58). The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating risk scores of different answers.



$X^2(12) = 207.101$, $p<0.001$

Figure 3.7: Medical practitioners' mean rating scores when assessing the risks associated with prescribing of statins by pharmacists (N=62)

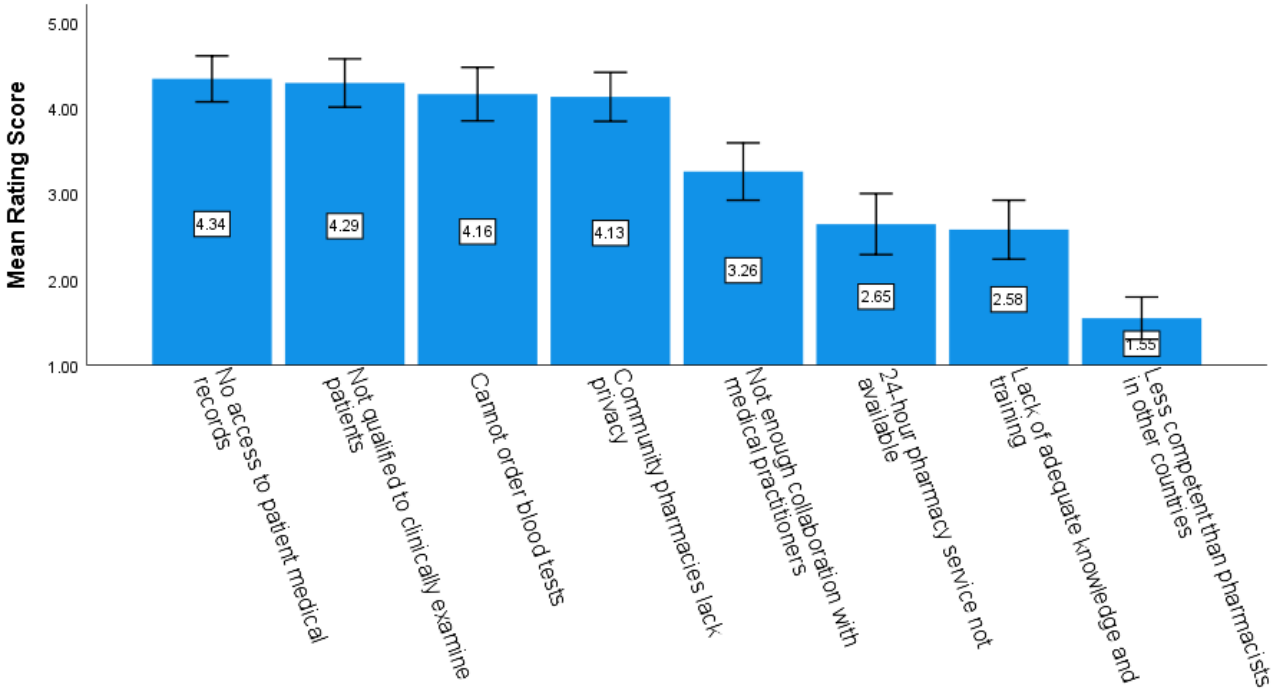
Forty-two medical practitioners (67.7%) thought that pharmacists should not be given statin prescribing rights, while 20 medical practitioners (32.3%) supported prescribing of statins by pharmacists.

The association between years of experience and opinion of medical practitioners whether pharmacists should be given statin prescribing rights was analysed (Table 3.3). The Chi-square test did not show a statistically significant association (p=0.475), indicating that years of experience did not significantly influence the attitude towards pharmacists prescribing statins.

Table 3.3: Association between medical practitioners' years of experience and attitude towards pharmacists' statin prescribing rights (N=62)

Medical practitioners' years of experience	Whether pharmacists in Malta should be given statin prescribing rights?	n	%	p-value
Less than or equal to 20 years	Yes	7	38.9	0.475
	No	11	61.1	
More than 20 years	Yes	13	29.5	
	No	31	70.5	

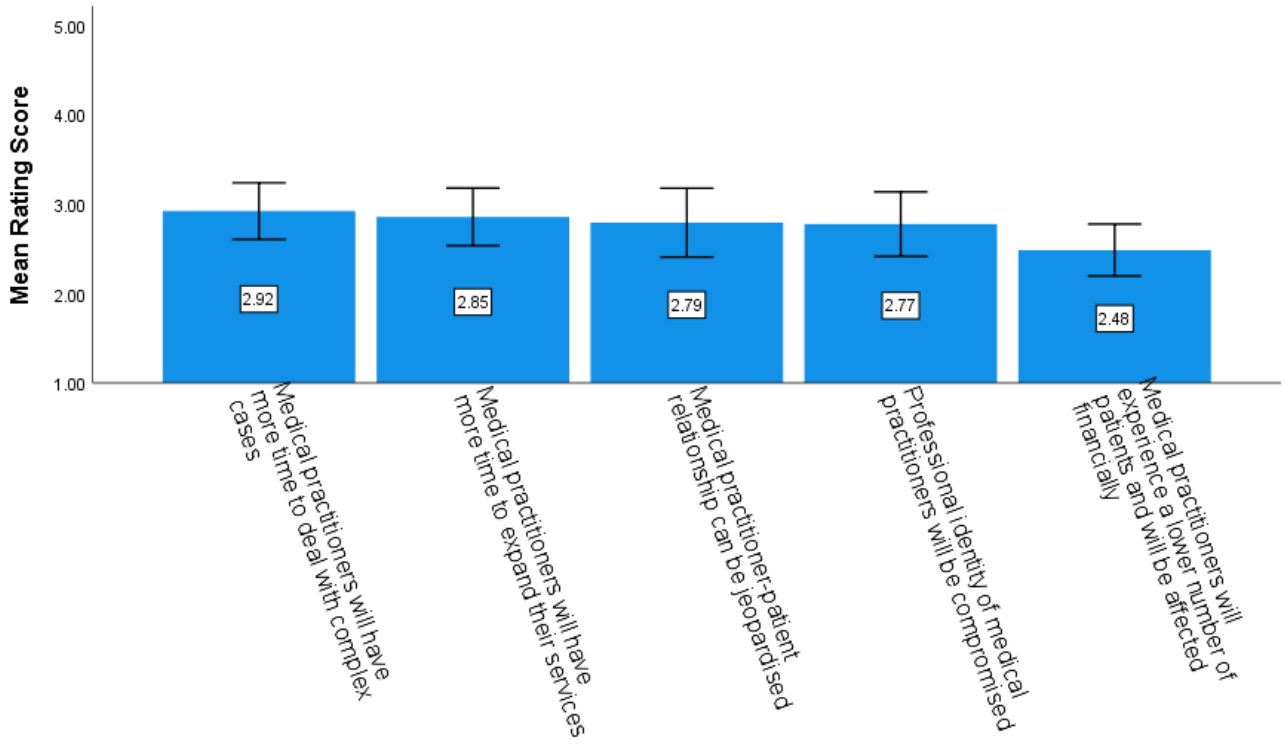
Reasons why medical practitioners in this study thought that pharmacists in Malta should not be given statin prescribing rights like pharmacists in other countries, were: 'pharmacists in Malta do not have access to patient medical records' (n=38, 61.3%), 'pharmacists in Malta are not qualified to clinically examine patients' (n=37, 59.7%), 'pharmacists in Malta cannot order blood tests to monitor patient outcomes' (n=35, 56.4%) and 'community pharmacies in Malta lack privacy'. Confidentiality of patient data might be endangered because of possible improper communication between the pharmacist and the patient' (n=32, 51.6%). Figure 3.8 represents the mean rating scores of all the reasons why pharmacist in Malta should not be given statin prescribing rights. The highest mean rating score (4.34) was assigned to 'pharmacists in Malta do not have access to patient medical records', while the lowest mean rating score (1.55) was given to 'pharmacists in Malta are less competent and have less knowledge than pharmacists in other countries who can prescribe'. The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating scores of different answers.



$X^2(7) = 232.131$, $p<0.001$

Figure 3.8: Medical practitioners' mean rating scores representing the level of agreement with the reasons why pharmacists in Malta should not be given statin prescribing rights (N=62)

If pharmacists are given the right to prescribe statins, 12 medical practitioners (19.4%) strongly agreed with the statement 'medical practitioner-patient relationship can be jeopardised', while 10 (16.1%) strongly agreed with the statement 'professional identity of medical practitioners will be compromised'. Figure 3.9 represents the mean rating scores for level of agreement with different statements, using a scale of 1 (strongly disagree) to 5 (strongly agree). The highest level of agreement (2.92) was with the statement: 'medical practitioners will have more time to deal with complex cases'. The lowest level of agreement (2.48) was related to the statement: 'medical practitioners will experience a lower number of patients and will be affected financially'. The Friedman test did not show a statistically significant difference (p=0.067) amongst mean rating scores of different answers.



$X^2(4) = 8.780$, $p = 0.067$

Figure 3.9: Medical practitioners' mean rating scores representing the level of agreement with different statements if pharmacists are given right to prescribe statins (N=62)

When asked how much is the medical practitioner-pharmacist collaboration beneficial for the patient, the majority of medical practitioners (n=54, 87.1%) said it is beneficial. Of those, 42 medical practitioners (67.7%) chose 'very beneficial' which was assigned the value of 5, while 12 (19.4%) opted for value of 4. Three medical practitioners (4.8%) had a neutral opinion, while 5 medical practitioners (8.1%) thought that collaboration is not beneficial for the patient. Of those, 3 (4.8%) opted for value of 2, and 2 (3.3%) chose value of 1, 'not beneficial at all'.

The relationship between medical practitioners' years of experience and their opinion about pharmacists' competence to prescribe statins and benefits of medical practitioner-pharmacist collaboration was analysed (Table 3.4). The Kruskal Wallis test did not show

statistically significant relationships (p=0.585 and p=0.481 respectively), indicating that medical practitioners' years of experience did not significantly influence their opinion about pharmacists' competence to prescribe statins neither their opinion about benefits of medical practitioner-pharmacist collaboration.

Table 3.4: The relationships between medical practitioners' years of experience and: a) their opinion about pharmacists' competence to prescribe statins, b) their opinion about benefits of medical practitioner-pharmacist collaboration (N=62)

	Medical practitioners' years of experience	**n**	**Mean rating score**	**Standard deviation**	**p-value**
Pharmacists' competence to prescribe statins	Less than or equal to 20 years	18	3.00	0.907	0.585
	More than 20 years	44	2.82	1.244	
Benefits of medical practitioner-pharmacist collaboration	Less than or equal to 20 years	18	4.67	0.594	0.481
	More than 20 years	44	4.34	1.140	

Forty-eight medical practitioners (77.4%) said they routinely collaborate with the pharmacist in their medical practice, while 14 (22.6%) said they do not. The association between medical practitioners' years of experience and whether they routinely collaborate with the pharmacist was analysed (Table 3.5) using the Chi-square test. No statistically significant association (p=0.195) was found, indicating that years of experience did not significantly influence on their collaboration.

Table 3.5: The association between medical practitioners' years of experience and their collaboration with the pharmacists (N=62)

Medical practitioners' years of experience	Do you routinely collaborate with a pharmacist in your medical practice?	n	%	p-value
Less than or equal to 20 years	Yes	12	66.7	0.195
	No	6	33.3	
More than 20 years	Yes	36	81.8	
	No	8	18.2	

Kruskal Wallis (Table 3.6) or Chi-square test (Table 3.7) were used to analyse whether collaboration of medical practitioners with pharmacists influences their opinion regarding pharmacists' competence to prescribe statins, potential prescribing rights and benefits of collaboration.

The Kruskal Wallis test did not show a statistically significant relationship (p=0.474) between medical practitioners' collaboration with pharmacists and their opinion about pharmacists' competence to prescribe statins. Neither was there a statistically significant relationship (p=0.142) between medical practitioners' collaboration with pharmacists and their opinion about benefits of medical practitioner-pharmacist collaboration, indicating that medical practitioners' collaboration with the pharmacists did not significantly influence their opinion about pharmacists' competence to prescribe statins neither on opinion about benefits of that collaboration.

Table 3.6: The relationship between medical practitioners' collaboration with pharmacists and: a) their opinion about pharmacists' competence to prescribe statins, b) their opinion about benefits of medical practitioner-pharmacist collaboration (N=62)

	Do you routinely collaborate with a pharmacist in your medical practice?	n	Mean rating score	Standard deviation	p-value
Pharmacists' competence to prescribe statins	Yes	48	2.81	1.161	0.474
	No	14	3.07	1.141	
Benefits of medical practitioner-pharmacist collaboration	Yes	48	4.48	0.945	0.142
	No	14	4.29	1.267	

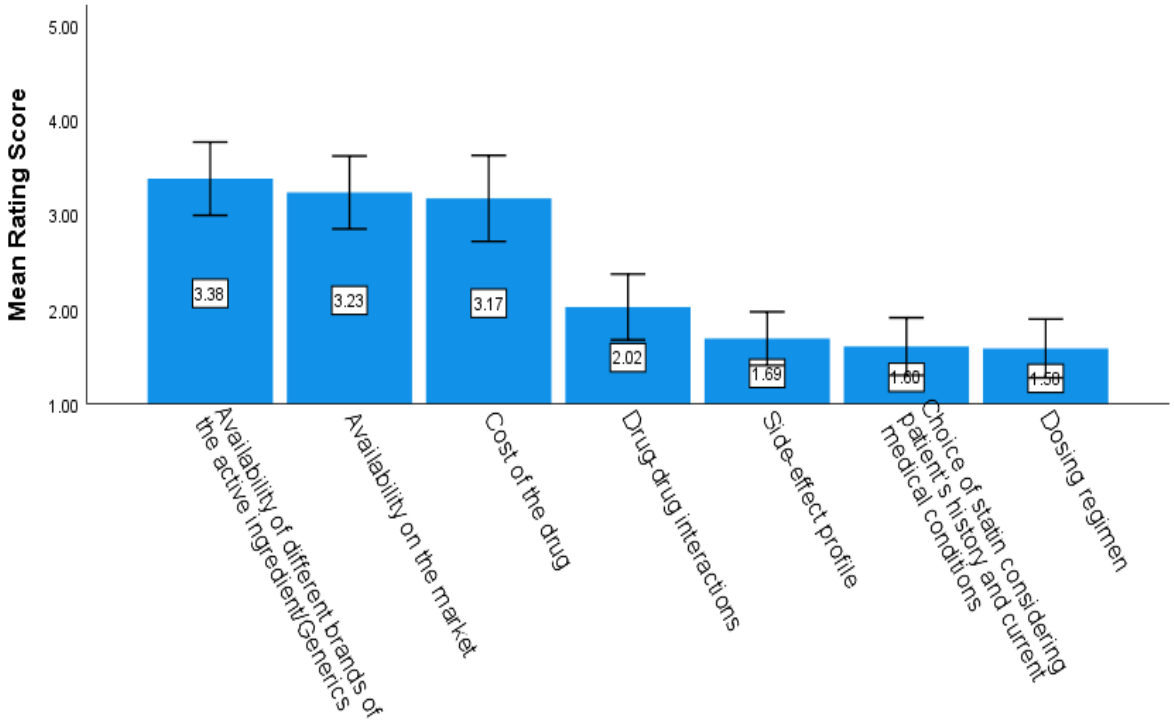
The Chi-square test did not show a statistically significant association (p=0.737) between medical practitioners' collaboration with pharmacists and their opinion whether pharmacists in Malta should be given statin prescribing rights.

Table 3.7: The association between medical practitioners' collaboration with pharmacists and their attitude towards pharmacists' statin prescribing rights (N=62)

Do you routinely collaborate with a pharmacist in your medical practice?	Whether pharmacists in Malta should be given statin prescribing rights?	n	%	p-value
Yes	Yes	16	33.3	0.737
	No	32	66.7	
No	Yes	4	28.6	
	No	10	71.4	

Medical practitioners who already collaborated with pharmacists (n=48, 77.4%) were asked how often they consult a pharmacist to discuss certain issues before prescribing statins. Thirteen medical practitioners (21%) said they 'always' consult the pharmacist

regarding the 'cost of the drug' and 12 (19.4%) 'always' consult the pharmacist regarding the 'availability of different brands of the active ingredient/generics'. Ten medical practitioners (16.1%) 'always' consult a pharmacist regarding 'availability on the market'. Figure 3.10 represents the mean rating scores regarding frequency of consultation of pharmacist by medical practitioner before prescribing statins, where 1 is 'never' and 5 is 'always'. The most frequent consultation was 'availability of different brands of the active ingredient/generics' (3.38), while the least frequent consultation prior to statin prescribing was 'dosing regimen' (1.58). The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating scores of different answers.



$X^2(6) = 176.511$, $p<0.001$

Figure 3.10: Frequency of consultation with pharmacists by medical practitioners prior to prescribing of statins, medical practitioners' perspective (N=62)

From 14 medical practitioners (22.6%) who said they do not routinely collaborate with the pharmacist in their medical practice, 12 (85.7%) said they were willing to start collaborating, while 2 (14.3%) were not. Those who were not willing stated reasons: "*Due to time restrictions*" and "*Pharmacist must be on 24-hour roster with the doctor, both should have dedicated contact lines, better infrastructure and medical record keeping needed, I would not accept ultimate responsibility of patients being treated by pharmacist*".

When asked to rate the importance of the factors that could promote a smooth implementation of pharmacist prescribing in Malta, 51 medical practitioners (82.3%) thought that 'community pharmacy setting needs to guarantee patient privacy and confidentiality' was very important, while 50 (80.6%) said that 'good collaboration with medical practitioners is vital' was very important. These were followed by: 'the medical condition needs to be diagnosed by a medical practitioner' (n=45, 72.6%), 'the prescribing and dispensing roles of pharmacists need to be separated so conflict of interest can be avoided' (n=44, 71%) and 'continuing professional development by pharmacists is essential' (n=40, 64.5%). Table 3.8 represents the mean rating scores of importance of all the factors that could promote a smooth implementation of pharmacist prescribing in Malta. The most important factor was 'community pharmacy setting needs to guarantee patient privacy and confidentiality' (4.74), while the least important was '24-hour pharmacy service should be available in Malta' (3.24). The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating scores of different answers.

Table 3.8: Medical practitioners' mean rating scores when rating the importance of the factors that could promote a smooth implementation of pharmacist prescribing in Malta (N=62)

Factors that promote a smooth implementation of pharmacist prescribing in Malta	**Mean rating score**	**Standard deviation**
Community pharmacy setting needs to guarantee patient privacy and confidentiality	4.74	0.676
Good collaboration with medical practitioners is vital	4.71	0.710
The medical condition needs to be diagnosed by a medical practitioner	4.48	1.004
Continuing professional development by pharmacists is essential	4.40	1.047
The prescribing and dispensing roles of pharmacists need to be separated so conflict of interest can be avoided	4.35	1.189
Clinical supervision by a medical practitioner is crucial	4.13	1.123
Management and other team members in community pharmacies/hospitals need to be supportive and organised, so pharmacists have the time to perform prescribing	4.05	1.311
The programme of pharmacist education at the University of Malta needs to address study units aimed towards pharmacist prescribing	4.03	1.355
Specialised training courses for pharmacists to undertake additional prescribing role need to be organised	3.98	1.408
Pharmacist prescribers need to be adequately remunerated	3.58	1.362
Pharmacist prescribing needs to be recognised as a positive contributor to patient management from all healthcare professionals	3.45	1.387
Access to electronic medical records needs to be given to pharmacists	3.32	1.617
A structured system should be in place to facilitate routine follow-up of patients by pharmacists for outcomes (example, pharmacists ordering blood tests)	3.24	1.586
24-hour pharmacy service should be available in Malta	3.24	1.512

$X^2(13) = 154.777$, $p<0.001$

3.3 Analysis of SPQ_{Pharm}

The SPQ_{Pharm} was completed by 152 pharmacists, where 109 pharmacists completed the questionnaire during personal visits (response rate 64.1%) and 43 completed it online. Four questionnaires were incomplete leaving 148 questionnaires which were included in the final analysis. Since in Malta there was 1250 registered pharmacists at the time of questionnaires distribution, a 7% margin of error was obtained.

Forty-four pharmacists (29.7%) had 20 years of professional experience, which was followed by 34 pharmacists (23%) who had 2-5 years of professional experience, 27 pharmacists (18.2%) with 6-11 years of experience, 23 (15.5%) with 11-20 years and finally 20 (13.5%) with less than 2 years of professional experience.

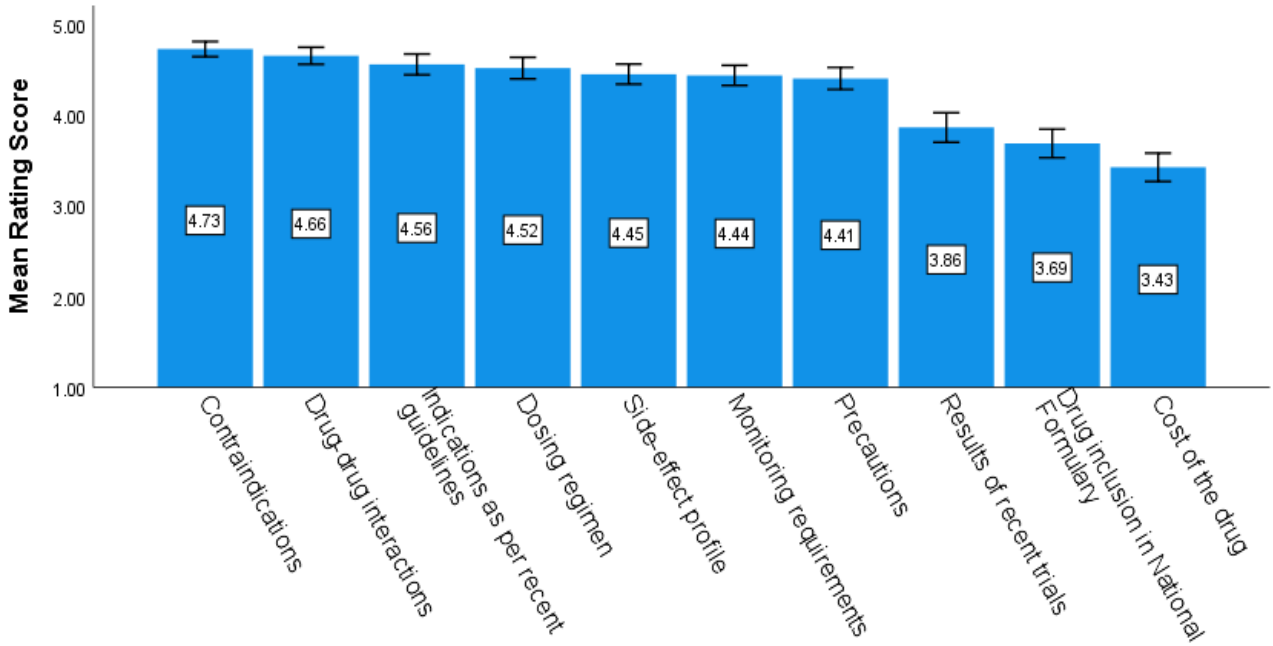
The majority of those who completed the questionnaire (n=114, 77%) were working in a community pharmacy. Sixteen pharmacists (10.8%) were working in regulatory sciences. Twelve pharmacists (8%) were working in a hospital. Two pharmacists (1.4%) worked in academia and 2 (1.4%) were working in pharmaceutical industry. Two pharmacists (1.4%) were working in a pharmaceutical company. Nine pharmacists (6.1%) were working as locums in a community pharmacy. Out of 148 pharmacists, 123 (83.1%) were working in a community pharmacy, either full-time or as locums.

The most frequent patient age group with whom pharmacists had contact was 19-65 years (n=125, 84.4%). Twenty-two pharmacists (14.9%) mostly had contact with patients older than 65 years, while 1 pharmacist (0.7%) was working mostly with patients $\leq$ 18 years.

When asked how many patients they encounter with hypercholesterolaemia and diabetes mellitus type 2 per week, 73 pharmacists (49.3%) were seeing between 10-30 patients with diabetes mellitus type 2 and 66 (44.6%) were seeing between 10-30 patients with

hypercholesterolaemia per week. This was followed by 30 pharmacists (20.3%) who encountered 31-50 patients with diabetes mellitus type 2 per week and 36 (24.3%) who encountered the same number of patients with hypercholesterolaemia per week. More than 50 patients with diabetes mellitus type 2 per week were seen by 23 pharmacists (15.5%), whilst more than 50 patients with hypercholesterolaemia per week were seen by 24 pharmacists (16.2%). Less than 10 patients with diabetes mellitus type 2 and hypercholesterolaemia were seen by 22 pharmacists (14.86%) per week.

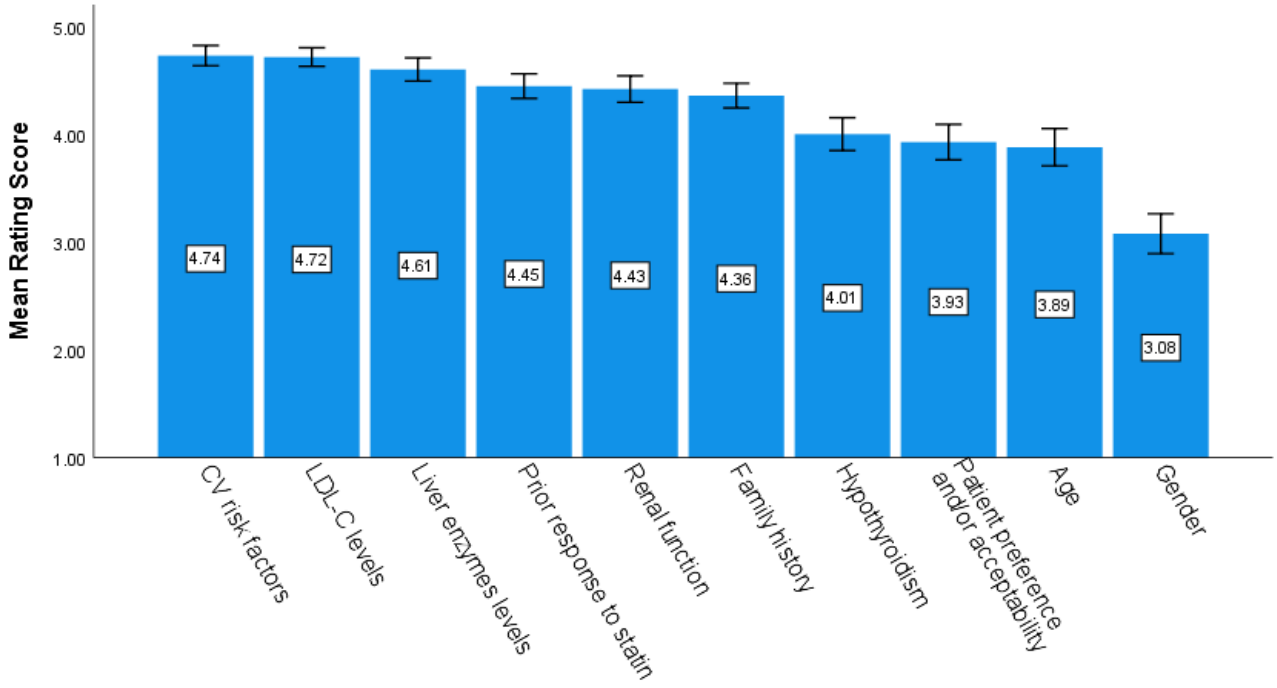
In order to evaluate pharmacists' awareness related to statin prescribing, the percentage of pharmacists who chose the highest rating score (5) on the Likert scale was assessed. When pharmacists were asked to rate the importance of drug-related information when statins are prescribed, 113 (76.4%) said that 'contraindications' are very important. This was followed by 105 pharmacists (70.9%) who replied that 'drug-drug interactions' are very important, while 99 (66.9%) rated 'indications as per recent guidelines' as very important. Ninety-five pharmacists (64.2%) rated 'dosing regimen' as very important, while 82 (55.4%) rated 'side-effect profile' as very important drug-related information. Figure 3.11 represents the mean rating scores for the importance of the drug-related information when statins are prescribed for primary prevention of ASCVD in patients with diabetes mellitus type 2 and/or hypercholesterolaemia. The highest mean rating score of 4.73 (out of 5) was assigned to 'contraindications' while the lowest was assigned to 'cost of the drug' (3.43). The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating scores of different answers.



$X^2(9) = 426.321$, $p<0.001$

Figure 3.11: Pharmacists' mean rating scores when rating the importance of the drug-related information when statins are prescribed (N=148)

When pharmacists were asked to rate the importance of patient-related information when statins are prescribed to patients with hypercholesterolaemia, 117 pharmacists (79%) said that 'CV risk factors' are very important. This was followed by 113 pharmacists (76.4%) who chose 'LDL-C levels' and 103 pharmacists (69.6%) who said that 'liver enzymes levels' are very important. Eighty-four pharmacists (56.8%) chose 'prior response to statin' and 83 (56.1%) rated 'renal function' as very important patient-related information when statins are prescribed. Figure 3.12 represents the mean rating scores for the importance of the patient-related information when statins are prescribed for primary prevention of ASCVD in patients with hypercholesterolaemia. The highest mean rating score (4.74) was assigned to 'CV risk factors' and the lowest (3.08) was assigned to 'gender'. The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating scores of different answers.

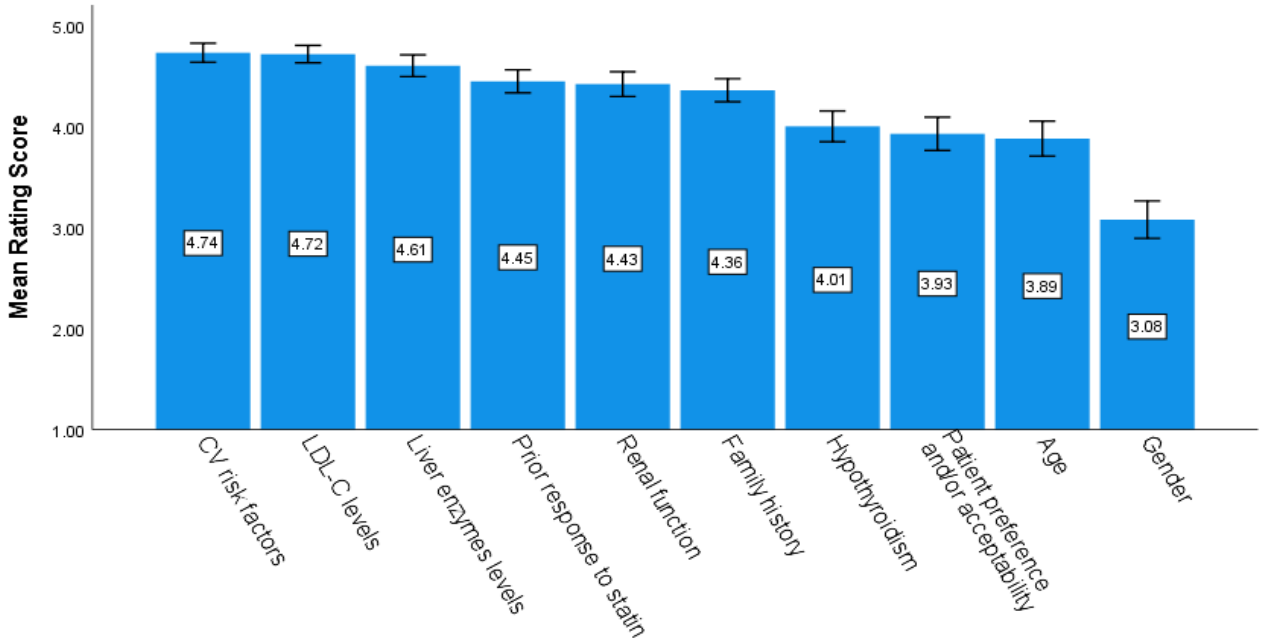


$X^2(9) = 485.430$, $p<0.001$

Figure 3.12: Pharmacists' mean rating scores when rating the importance of the patient-related information when statins are prescribed to patients with hypercholesterolaemia without previous ASCVD (N=148)

When pharmacists were asked to rate the importance of patient-related information when statins are prescribed to patients with diabetes mellitus type 2, 109 pharmacists (73.6%) said that 'CV risk factors' are very important. This was followed by 97 pharmacists (65.5%) who chose 'blood glucose/HbA1c levels' and 95 pharmacists (64.2%) who said that 'LDL-C levels' are very important. Ninety-four pharmacists (63.5%) chose 'liver enzymes levels and 84 (56.8%) rated 'renal function' as very important patient-related information when statins are prescribed. Figure 3.13 represent the mean rating scores for the importance of the patient-related information when statins are prescribed for primary prevention of ASCVD in patients with diabetes mellitus type 2. The highest mean rating score (4.70) was assigned to 'CV risk factors' and the lowest (3.48) was assigned to

'gender'. The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating scores of different answers.



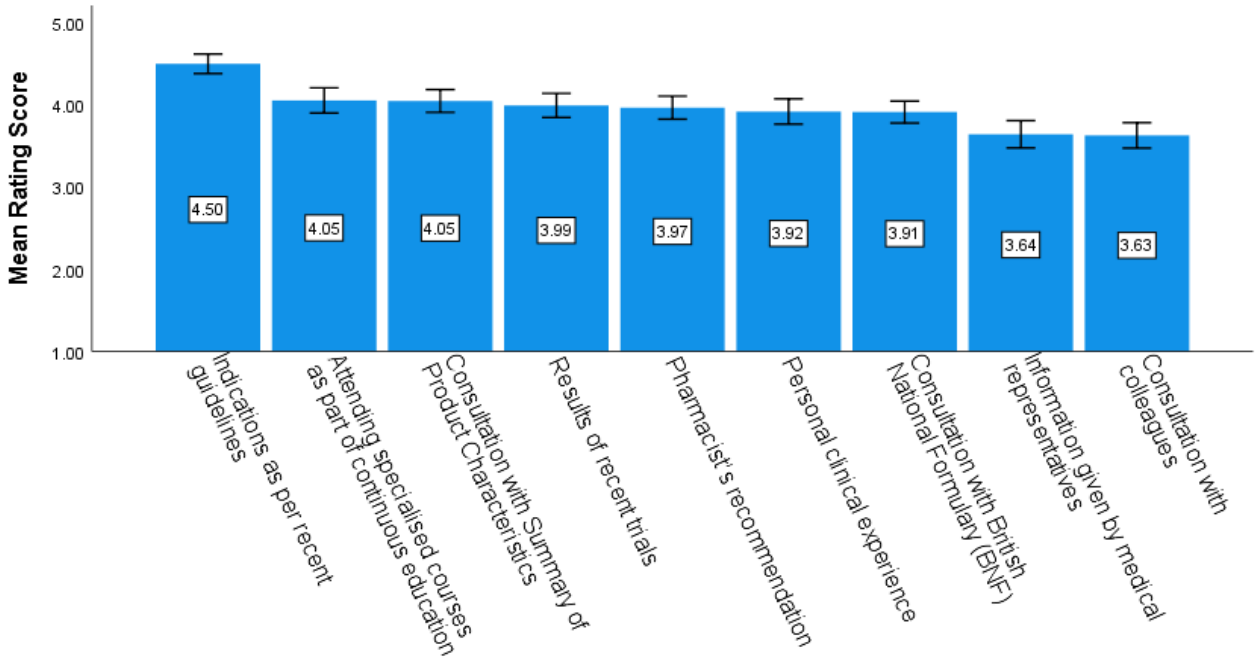
$X^2(10) = 340.647$, $p<0.001$

Figure 3.13: Pharmacists' mean rating scores when rating the importance of the patient-related information when statins are prescribed to patients with diabetes mellitus type 2 without previous ASCVD (N=148)

Pharmacists were asked how often should a patient's lipid-profile be monitored when statins are prescribed for patients with hypercholesterolaemia without previous ASCVD. Seventy-one pharmacists (48%) said that monitoring should be performed 'every 6 months', 36 (24.3%) 'every 3 months' and 31 (20.9%) said 'yearly'.

When statins are prescribed for patients with hypercholesterolaemia and/or diabetes mellitus type 2 without previous ASCVD, monitoring of the patient's liver function should be performed 'every 6 months' (n=55, 37.2%), 'every 3 months' (n=50, 33.8%), 'yearly' (n=24, 16.2%) and 'every 6 weeks' (n=10, 6.8%).

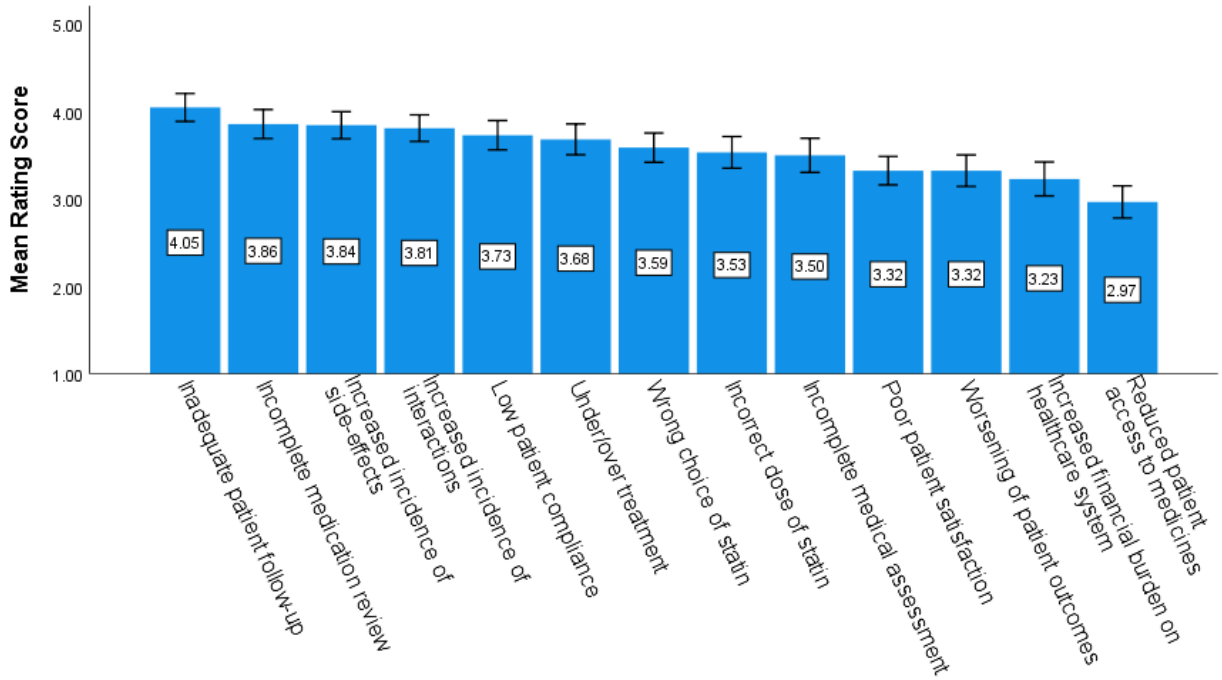
Pharmacists were asked to rate the importance of the factors that could influence the prescribing of statins. Ninety-three pharmacists (62.8%) chose 'indications as per recent guidelines', followed by 59 pharmacists (39.9%) who chose 'attending specialised courses as part of continuous education', 'consultation with Summary of Product Characteristics' (n=50, 33.8%), 'results of recent trials' (n=48, 32.4%) and 'personal clinical experience' (n=46, 31.1%). Figure 3.14 represents the mean rating scores for the importance of the factors that could influence the prescribing of statins. The highest mean rating score (4.50) was assigned to 'indications as per recent guidelines' and the lowest (3.63) was assigned to 'consultation with colleagues'. The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating scores of different answers.



$X^2(8) = 131.839$, $p<0.001$

Figure 3.14: Pharmacists' mean rating scores when rating the importance of the factors that could influence the prescribing of statins (N=148)

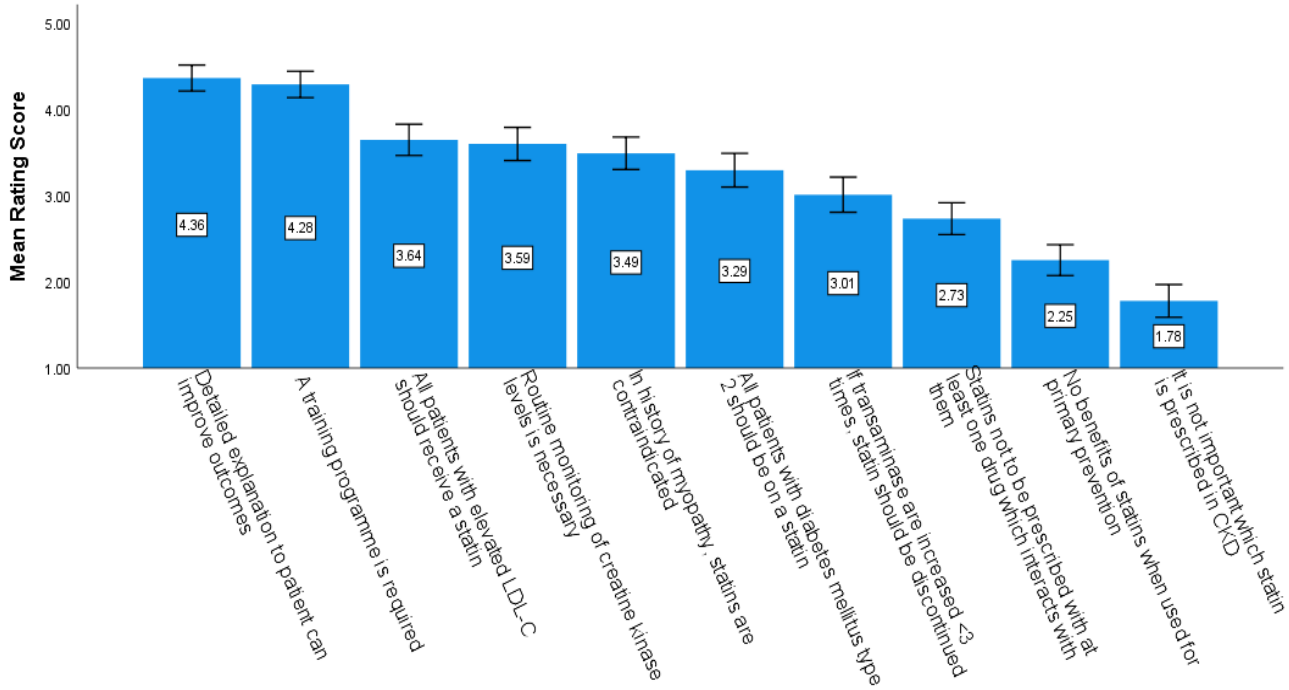
When assessing the risks associated with statin prescribing by medical practitioners (where 1 was low risk and 5 was high risk), 61 pharmacists (41.2%) thought that 'inadequate patient follow-up' present the high risk, while 46 pharmacists (31.1%) thought that 'incomplete medication review' is associated with high risk. This was followed by 'increased incidence of side-effects' and 'low patient compliance', both at 28.4% (n=42) and 'increased incidence of interactions' and 'under/over treatment' both at 26.4% (n=39). Figure 3.15 represents the mean rating risk scores associated with prescribing of statins by medical practitioners. Pharmacists thought that 'inadequate patient follow-up' represents the highest risk (4.05), while 'reduced patient access to medicines' represents the lowest risk (2.97). The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating risk scores of different answers.



$X^2(12) = 196.147$, $p<0.001$

Figure 3.15: Pharmacists' mean rating scores when assessing the risks associated with prescribing of statins by medical practitioners (N=148)

Pharmacists were asked to rate the level of agreement with specific statements regarding statin treatment, using scale of 1 to 5 where 1 was 'strongly disagree' and 5 'strongly agree'. Eighty-five pharmacists (57.4%) strongly agreed that 'detailed explanation to patient why statin is prescribed can improve outcomes', while 82 pharmacists (55.4%) strongly agreed with the statement 'an educational training programme on prescribing of statins is required'. Figure 3.16 represents the mean rating scores of agreement regarding different statements related to pharmacist prescribing. The highest level of agreement (4.36) was with the statement 'detailed explanation to patient why statin is prescribed can improve outcomes', while the lowest level of agreement (1.78) was related to 'it is not important which statin is prescribed to patients with chronic kidney disease (CKD)'. The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating scores of different answers.



$X^2(9) = 487.002$, $p<0.001$

Figure 3.16: Pharmacists' mean rating scores representing the level of agreement with different statements regarding prescribing of statins (N=148)

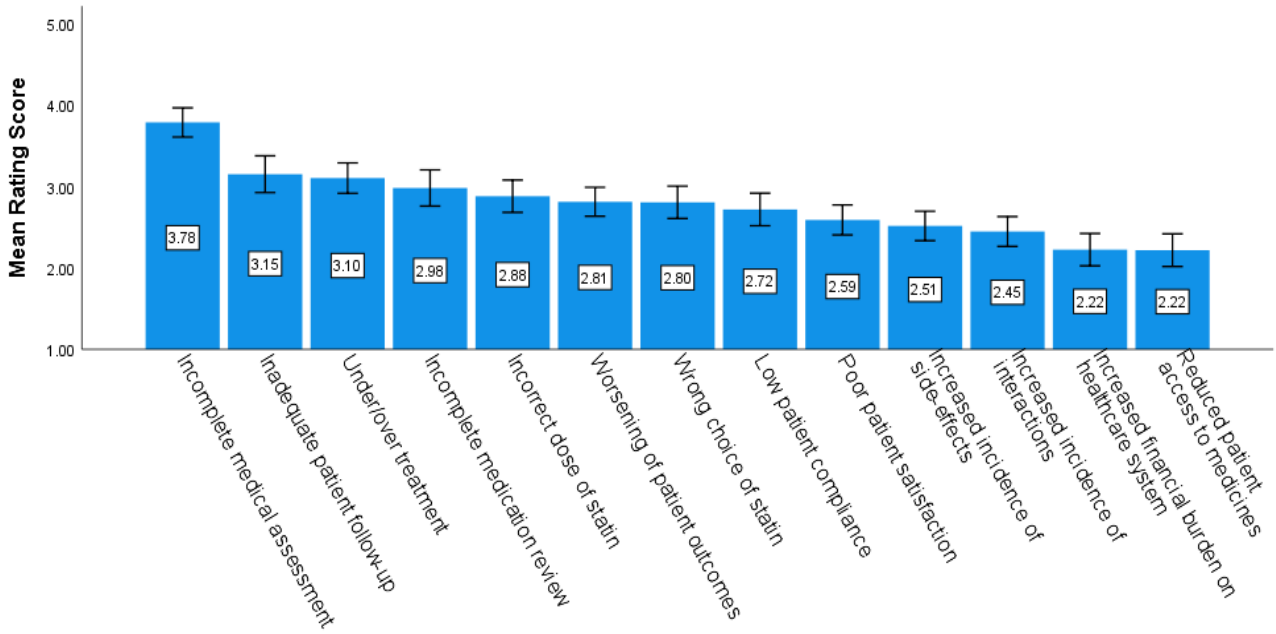
Table 3.9 represents the number of pharmacists who disagreed, had neutral opinion or agreed with different statements related to prescribing of statins.

Table 3.9: The number of pharmacists who agreed, had neutral opinion or disagreed with specific statements regarding prescribing of statins (N=148)

	Disagreement **Values 1 and 2** **n (%)**	**Neutral opinion** **Value 3** **n (%)**	**Agreement** **Values 4 and 5** **n (%)**
All patients with diabetes mellitus type 2, aged 40-75 years should be on a statin regardless of their LDL-C levels	39 (26.4)	37 (25)	72 (48.6)
All patients with elevated LDL-C, aged 40-75 years should receive a statin, regardless of their CVD risk	25 (16.9)	31 (20.9)	92 (62.2)
It is not important which statin is prescribed to patients with chronic kidney disease (CKD)	114 (77)	21 (14.2)	13 (8.8)
If transaminase levels are increased less than three times the upper limit of normal, statin should be discontinued	49 (33.1)	49 (33.1)	50 (33.8)
Routine monitoring of creatine kinase levels (as a sign of myopathy) is necessary even in asymptomatic patients	28 (18.9)	31 (20.9)	89 (60.2)
In patients with history of myopathy, statins are contraindicated	28 (18.9)	45 (30.4)	75 (50.7)
There is a lack of beneficial effect of statins when used for primary prevention in patients aged 40-75 years with hypercholesterolaemia and/or diabetes mellitus type 2	90 (60.8)	37 (25)	21 (14.2)
Statins should not be prescribed to patients who have at least one drug which interacts with statins (example, amlodipine)	61 (41.2)	53 (35.8)	34 (23)
Detailed explanation to patient why statin is prescribed, can improve outcomes	10 (6.8)	10 (6.8)	128 (86.4)
An educational training programme on prescribing of statins is required	8 (5.4)	23 (15.5)	117 (79.1)

When asked whether pharmacists are competent to prescribe statins, on the scale of 1 (not competent at all) to 5 (highly competent), 75 pharmacists (50.7%) thought that pharmacists are competent to prescribe statins (values 4 and 5 on Likert scale). Of those, 60 pharmacists (40.5%) chose the value of 4 and 15 (10.2%) rated the pharmacists' ability to prescribe as highly competent (5). Fifty-five pharmacists (37.2%) had a neutral opinion, while 18 pharmacists (12.2%) thought that pharmacists are not competent. Of those, 6 pharmacists (4.1%) assigned a value of 1 with respect to pharmacist competence whilst 12 pharmacists (8.1%) assigned the value of 2. The mean rating score of pharmacists' competence, by pharmacists, to prescribe statins for primary prevention, to a selected group of patients was 3.44.

When pharmacists were asked to assess the risks associated with prescribing of statins by pharmacists (where 1 was low risk and 5 was high risk), if prescribing rights are given to pharmacists in Malta, 46 pharmacists (31.1%) thought that 'incomplete medical assessment' is a high risk. This was followed by: 'inadequate patient follow-up' and 'incomplete medication review', both at 16.9% (n=25), 'under/over treatment' (n=18, 12.2%) and 'wrong choice of statin' (n=14, 9.5%). Figure 3.17 represents the mean rating risk scores associated with prescribing of statins by pharmacists. Pharmacists thought that 'incomplete medical assessment' represents the highest risk (3.78), while 'reduced patient access to medicines' represents the lowest risk (2.22). The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating risk scores of different answers.



$X^2(12) = 333.427$, $p<0.001$

Figure 3.17: Pharmacists' mean rating scores when assessing the risks associated with prescribing of statins by pharmacists (N=148)

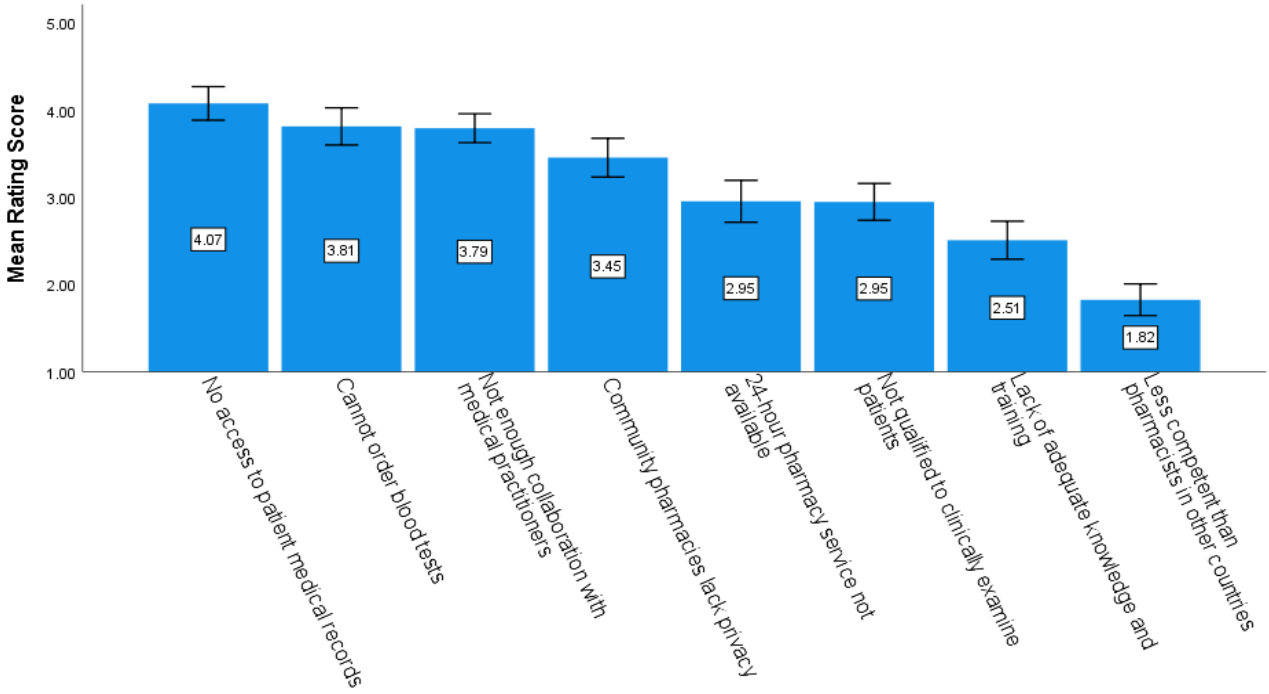
One hundred twenty-three pharmacists (83.1%) thought that pharmacists should be given statin prescribing rights, while 25 pharmacists (16.9%) opposed prescribing of statins by pharmacists.

The association between years of experience and pharmacists' opinion whether pharmacists should be given prescribing rights was analysed (Table 3.10). The Chi-square test did not show a statistically significant association (p=0.087) between years of experience of pharmacists and their opinion whether pharmacists in Malta should be given prescribing rights, indicating that years of experience did not significantly influence the attitude towards pharmacist prescribing statins.

Table 3.10: The association between pharmacists' years of experience and attitude towards pharmacists' statin prescribing rights (N=148)

Pharmacists' years of experience	Whether pharmacists in Malta should be given statin prescribing rights?	n	%	p-value
Less than or equal to 20 years	Yes	90	86.5	0.087
	No	14	13.5	
More than 20 years	Yes	33	75	
	No	11	25	

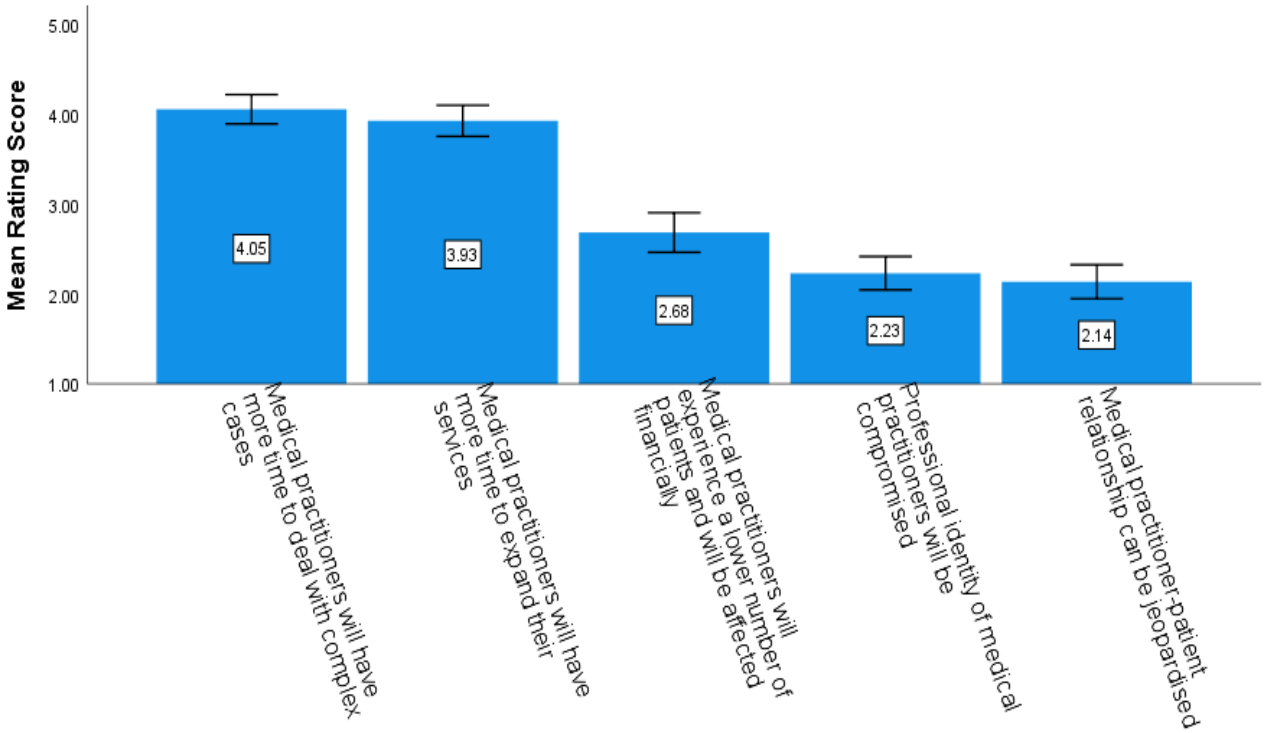
Pharmacists were asked to rate the statements why pharmacists in Malta should not be given statin prescribing rights like pharmacists in other countries. Seventy-five pharmacists (50.7%) strongly agreed with the statement 'pharmacists in Malta do not have access to patient medical records', while 62 pharmacists (41.9%) strongly agreed with the statement 'pharmacists in Malta cannot order blood tests to monitor patient outcomes'. These were followed by: 'in Malta, there is not enough collaboration between pharmacists and medical practitioners' (n=45, 30.4%), 'community pharmacies in Malta lack privacy. Confidentiality of the patient data might be endangered because of possible improper communication between the pharmacist and the patient' (n=43, 29%) and '24-hour pharmacy service not available in Malta' (n=33, 22.3%). Figure 3.18 represents the mean rating scores of all the reasons why pharmacists in Malta should not be given prescribing rights. One of the main reasons identified with the highest mean rating score (4.07) was assigned to 'pharmacists in Malta do not have access to patient medical records'. The least agreement, with the lowest mean rating score (1.82), was associated with 'pharmacists in Malta are less competent and have less knowledge than pharmacists in other countries who can prescribe'. The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating scores of different answers.



$X^2(7) = 322.984$, $p < 0.001$

Figure 3.18: Pharmacists' mean rating scores representing the level of agreement with the reasons why pharmacists in Malta should not be given statin prescribing rights (N=148)

If pharmacists are given the right to prescribe statins, 62 pharmacists (41.9%) strongly agreed with the statement 'medical practitioners will have more time to deal with complex cases', while 57 (38.5%) strongly agreed with the statement 'medical practitioners will have more time to expand their services'. Figure 3.19 represents the mean rating scores for different statements, using a scale of 1 (strongly disagree) to 5 (strongly agree). The highest level of agreement (4.05) was with the statement: 'medical practitioners will have more time to deal with complex cases'. The lowest level of agreement (2.14) was related to the statement: 'medical practitioner-patient relationship can be jeopardised'. The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating scores of different answers.



$X^2(4) = 273.210$, $p<0.001$

Figure 3.19: Pharmacists' mean rating scores representing the level of agreement with different statements if pharmacists are given right to prescribe statins (N=148)

When asked how much is the medical practitioner-pharmacist collaboration beneficial for the patient, on a scale of 1 to 5 (1 is not beneficial at all while 5 is very beneficial), 145 pharmacists (98%) thought that collaboration is beneficial. Of those, 20 pharmacists (13.5%) assigned the value of 4 and 125 pharmacists (84.5%) thought that this relationship is very beneficial (5). Three pharmacists (2%) had neutral opinion.

The relationship between pharmacists' years of experience and their opinion about pharmacist's competence to prescribe statins and about benefits of medical practitioner-pharmacist collaboration was analysed (Table 3.11). The Kruskal Wallis test showed a statistically significant relationship (p=0.038) between pharmacists' years of experience and their opinion about pharmacists' competence to prescribe. Those pharmacists with

less than or equal to 20 years of experience thought that pharmacists are more competent to prescribe statins than pharmacists with more than 20 years of experience.

The Kruskal Wallis test did not show a statistically significant relationship (p=0.258) between pharmacists' years of experience and their opinion about benefits of medical practitioner-pharmacist collaboration, indicating that years of experience did not significantly influence on opinion about benefits of that collaboration.

Table 3.11: The relationships between pharmacists' years of experience and: a) their opinion about pharmacists' competence to prescribe statins, b) their opinion about benefits of medical practitioner-pharmacist collaboration (N=148)

	Pharmacists' years of experience	**n**	**Mean rating score**	**Standard deviation**	**p-value**
Pharmacists' competence to prescribe statins	Less than or equal to 20 years	104	3.55	0.912	**0.038**
	More than 20 years	44	3.20	0.930	
Benefits of medical practitioner-pharmacist collaboration	Less than or equal to 20 years	104	4.86	0.380	0.258
	More than 20 years	44	4.75	0.534	

Pharmacists were asked whether they routinely collaborate with a medical practitioner in their daily practice. Ninety-two pharmacists (62.2%) answered yes, while the remaining 56 pharmacists (37.8%) said no.

The association between pharmacists' years of experience and whether they routinely collaborate with the medical practitioner was analysed (Table 3.12). The Chi-square test did not show a statistically significant association (p=0.810), indicating that years of experience did not significantly influence their collaboration.

Table 3.12: The association between pharmacists' years of experience and their collaboration with the medical practitioners (N=148)

Pharmacists' years of experience	Do you routinely collaborate with a medical practitioner in your daily practice?	n	%	p-value
Less than or equal to 20 years	Yes	64	61.5	0.810
	No	40	38.5	
More than 20 years	Yes	28	63.6	
	No	16	36.4	

The Kruskal Wallis (Table 3.13) and Chi-square test (Table 3.14) were done to analyse whether collaboration of pharmacists with medical practitioners influence their opinion regarding pharmacists' competence to prescribe statins, potential prescribing rights and benefits of collaboration.

The Kruskal Wallis test showed a statistically significant relationship (p=0.019) between pharmacists' routine collaboration with medical practitioners and their opinion about pharmacists' competence to prescribe statins. Pharmacists who collaborated with medical practitioners thought that pharmacists are more competent to prescribe statins than pharmacists who do not collaborate routinely with medical practitioners.

The Kruskal Wallis test did not show a statistically significant relationship (p=0.101) between pharmacists' routine collaboration with medical practitioners and pharmacists' opinion about benefits of medical practitioner-pharmacist collaboration, indicating that routine collaboration did not significantly influence on pharmacists' opinion about benefits of that collaboration.

Table 3.13: The relationship between pharmacists' collaboration with medical practitioners and: a) their opinion about pharmacists' competence to prescribe statins, b) their opinion about benefits of medical practitioner-pharmacist collaboration (N=148)

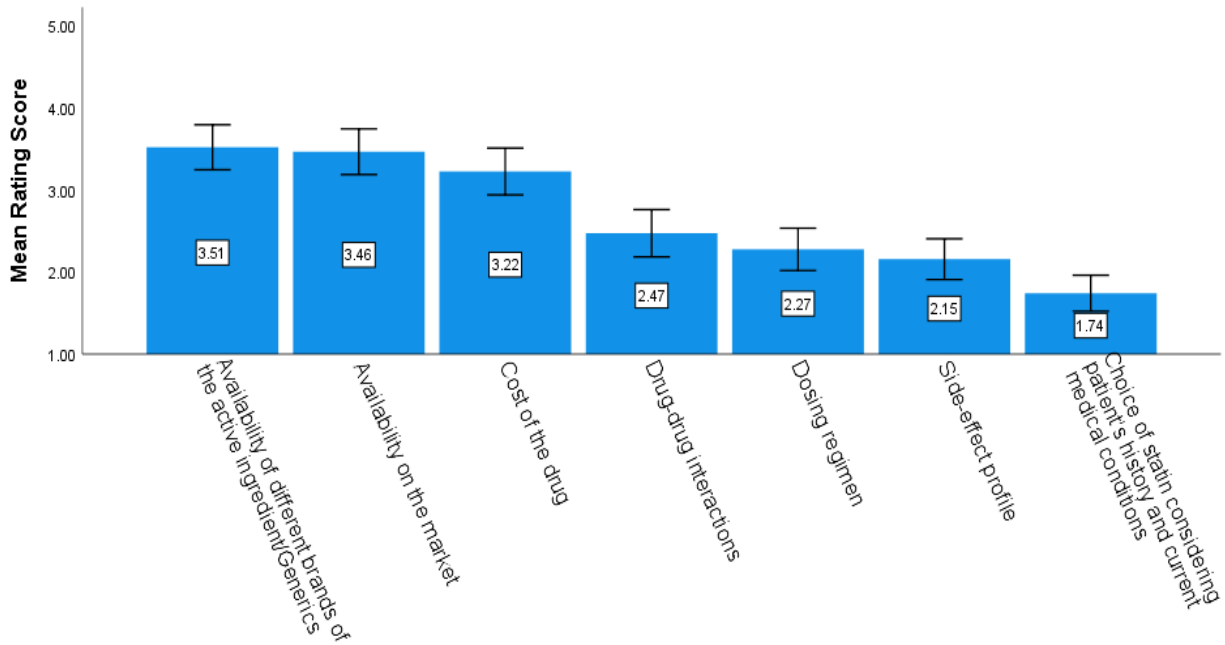
	Do you routinely collaborate with a medical practitioner in your daily practice?	n	Mean rating score	Standard deviation	p-value
Pharmacists' competence to prescribe statins	Yes	92	3.59	0.891	**0.019**
	No	56	3.21	0.948	
Benefits of medical practitioner-pharmacist collaboration	Yes	92	4.88	0.326	0.101
	No	56	4.73	0.556	

The Chi-square test did not show a statistically significant association (p=0.109) between pharmacists' routine collaboration with medical practitioners and their opinion about whether pharmacists should be given statin prescribing rights, indicating that routine collaboration did not significantly influence on pharmacists' opinion whether pharmacists should be given statin prescribing rights.

Table 3.14: The association between pharmacists' collaboration with medical practitioners and their attitude towards pharmacists' statin prescribing rights (N=148)

Do you routinely collaborate with a medical practitioner in your daily practice?	Whether pharmacists in Malta should be given statin prescribing rights?	n	%	p-value
Yes	Yes	80	87	0.109
	No	12	13	
No	Yes	43	76.8	
	No	13	23.2	

Pharmacists who collaborate daily with medical practitioners (n=92, 62.2%) were asked to estimate the frequency of consultation for specific issues before statins are prescribed by medical practitioners. Twenty-three pharmacists (25%) said they are 'always' consulted regarding 'availability of different brands of the active ingredient/generics'. This was followed by the 'availability on the market' (n=21, 22.8%) and 'cost of the drug' (n=17, 18.5%). Figure 3.20 represents the mean rating scores regarding frequency of consultation of pharmacists by medical practitioners before statins are prescribed, where 1 is 'never' and 5 is 'always'. The most frequent consultation was 'availability of different brands of the active ingredient/generics' (3.51), while the least frequent consultation prior to statin prescribing was 'choice of statin considering patient's history and current medical conditions' (1.74). The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating scores of different answers.



$X^2(6) = 229.711$, $p<0.001$

Figure 3.20: Frequency of consultation with pharmacists by medical practitioners prior to prescribing of statins, pharmacists' perspective (N=148)

Pharmacists who do not routinely collaborate with medical practitioners in their daily practice (n=56, 37.8%) were asked whether they are willing to start collaborating with a medical practitioner. Fifty-four (96.4%) answered 'yes' while 2 (3.6%) said 'no'. Pharmacists who replied in the negative said that reasons include: "*Lack confidence to give clinical advice due to lack of clinical experience*" and "*At the pharmacy I practice I do not have a doctor present so it is difficult to collaborate with the doctor over the phone. In a pharmacy where is a doctor present we used to discuss prices and treatment options*".

Pharmacists were asked to rate the importance of the factors that could promote a smooth implementation of pharmacist prescribing in Malta, on a scale of 1 to 5, where 1 is 'not important at all' and 5 is 'very important'. One hundred and twenty-two pharmacists (82.4%) thought that 'access to electronic medical records needs to be given to pharmacists' is very important, while 121 pharmacists (81.8%) said that 'the programme of pharmacist education at the University of Malta needs to address study units aimed towards pharmacist prescribing' is very important. These were followed by: 'a structured system should be in place to facilitate routine follow-up of patients by pharmacists for outcomes (example, pharmacists ordering blood tests)' (n=118, 79.7%), 'specialised training courses for pharmacists to undertake additional prescribing role need to be organised' (n=115, 77.7%) and 'management and other team members in community pharmacies/hospitals need to be supportive and organised, so pharmacists have the time to perform prescribing' (n=109, 73.6%). Table 3.15 represents the mean rating scores of the factors that could promote a smooth implementation of pharmacist prescribing in Malta. The most important factor that could promote a smooth implementation of pharmacist prescribing was 'access to electronic medical records needs to be given to pharmacists' (4.80). The least important factor was '24-hour pharmacy service should be

available in Malta' (3.15). The Friedman test showed that there was a statistically significant difference ($p<0.001$) amongst mean rating scores of different answers.

Table 3.15: Pharmacists' mean rating scores when rating the importance of the factors that could promote a smooth implementation of pharmacist prescribing in Malta (N=148)

Factors that promote a smooth implementation of pharmacist prescribing in Malta	**Importance score**	**Standard deviation**
Access to electronic medical records needs to be given to pharmacists	4.80	0.466
A structured system should be in place to facilitate routine follow-up of patients by pharmacists for outcomes (example, pharmacists ordering blood tests)	4.76	0.500
The programme of pharmacist education at the University of Malta needs to address study units aimed towards pharmacist prescribing	4.75	0.605
Management and other team members in community pharmacies/hospitals need to be supportive and organised, so pharmacists have the time to perform prescribing	4.69	0.558
Good collaboration with medical practitioners is vital	4.64	0.608
Specialised training courses for pharmacists to undertake additional prescribing role need to be organised	4.64	0.774
Continuing professional development by pharmacists is essential	4.63	0.642
Community pharmacy setting needs to guarantee patient privacy and confidentiality	4.62	0.674
Pharmacist prescribing needs to be recognised as a positive contributor to patient management from all healthcare professionals	4.62	0.632
Pharmacist prescribers need to be adequately remunerated	4.54	0.768
The medical condition needs to be diagnosed by a medical practitioner	3.89	1.089
The prescribing and dispensing roles of pharmacists need to be separated so conflict of interest can be avoided	3.61	1.317
Clinical supervision by a medical practitioner is crucial	3.53	1.226
24-hour pharmacy service should be available in Malta	3.15	1.483

$X^2(13) = 560.293$, $p<0.001$

3.4 SPQ_{MedPr} and SPQ_{Pharm}: A Comparison

Opinions and attitudes of medical practitioners and pharmacists were compared.

When asked to rate the importance of drug-related information when statins are prescribed, there were no statistically significant differences in the mean rating scores between the two groups of healthcare professionals (Table 3.16).

Table 3.16: Medical practitioners (N=62) and pharmacists (N=148) mean rating scores when rating the importance of drug-related information when statins are prescribed

Drug Information	Healthcare professional	Mean rating score	Standard deviation	p-value
Indications as per recent guidelines	Medical practitioners	4.50	0.784	0.981
	Pharmacists	4.56	0.702	
Results of recent trials	Medical practitioners	3.85	1.038	0.074
	Pharmacists	3.86	1.001	
Dosing regimen	Medical practitioners	4.29	0.912	0.488
	Pharmacists	4.52	0.733	
Contraindications	Medical practitioners	4.63	0.707	0.142
	Pharmacists	4.73	0.516	
Precautions	Medical practitioners	4.29	0.894	0.460
	Pharmacists	4.41	0.745	
Monitoring requirements	Medical practitioners	4.02	0.983	0.388
	Pharmacists	4.44	0.682	
Side-effect profile	Medical practitioners	4.26	0.867	0.511
	Pharmacists	4.45	0.683	
Drug-drug interactions	Medical practitioners	4.50	0.763	0.095
	Pharmacists	4.66	0.580	
Cost of the drug	Medical practitioners	3.47	0.953	0.488
	Pharmacists	3.43	0.962	
Drug inclusion in National Formulary	Medical practitioners	3.47	1.238	0.232
	Pharmacists	3.69	0.975	

There were no statistically significant differences amongst any options when both healthcare professionals were asked to rate the importance of the patient-related information for patients with hypercholesterolaemia, prior to prescribing of statins (Table 3.17).

Table 3.17: Medical practitioners (N=62) and pharmacists (N=148) mean rating scores when rating the importance of the patient-related information when statins are prescribed to patients with hypercholesterolaemia without previous ASCVD

Patient Information	Healthcare professional	Mean rating score	Standard deviation	p-value
Age	Medical practitioners	3.95	0.999	0.092
	Pharmacists	3.88	1.066	
Gender	Medical practitioners	2.97	1.187	0.760
	Pharmacists	3.08	1.140	
CV risk factors	Medical practitioners	4.81	0.474	0.579
	Pharmacists	4.74	0.576	
LDL-C levels	Medical practitioners	4.63	0.607	0.672
	Pharmacists	4.72	0.532	
Liver enzymes levels	Medical practitioners	4.37	0.834	0.967
	Pharmacists	4.61	0.666	
Renal function	Medical practitioners	3.68	1.156	0.857
	Pharmacists	4.42	0.757	
Hypothyroidism	Medical practitioners	3.64	1.057	0.980
	Pharmacists	4.01	0.937	
Prior response to statin	Medical practitioners	4.11	0.943	0.075
	Pharmacists	4.45	0.703	
Family history	Medical practitioners	4.45	0.761	0.231
	Pharmacists	4.36	0.701	
Patient preference and/or acceptability	Medical practitioners	3.85	0.989	0.360
	Pharmacists	3.93	1.015	

There were no statistically significant differences when rating the importance of patient-related information prior to prescribing statins for patients with diabetes mellitus type 2, between the two groups of healthcare professionals (Table 3.18).

Table 3.18: Medical practitioners (N=62) and pharmacists (N=148) mean rating scores when rating the importance of the patient-related information when statins are prescribed to patients with diabetes mellitus type 2 without previous ASCVD

Patient Information	**Healthcare professional**	**Mean rating score**	**Standard deviation**	**p-value**
Age	Medical practitioners	3.87	1.123	0.084
	Pharmacists	4.06	0.984	
Gender	Medical practitioners	3.26	1.280	0.671
	Pharmacists	3.48	1.116	
CV risk factors	Medical practitioners	4.68	0.701	0.914
	Pharmacists	4.70	0.528	
LDL-C levels	Medical practitioners	4.58	0.821	0.905
	Pharmacists	4.53	0.751	
Blood glucose/HbA1c levels	Medical practitioners	4.47	1.004	0.671
	Pharmacists	4.56	0.682	
Liver enzymes levels	Medical practitioners	4.29	0.876	0.644
	Pharmacists	4.55	0.663	
Renal function	Medical practitioners	3.89	1.132	0.410
	Pharmacists	4.47	0.664	
Hypothyroidism	Medical practitioners	3.60	1.137	0.621
	Pharmacists	4.05	0.875	
Prior response to statin	Medical practitioners	4.10	0.936	0.247
	Pharmacists	4.22	0.900	
Family history	Medical practitioners	4.32	0.988	0.225
	Pharmacists	4.36	0.710	
Patient preference and/or acceptability	Medical practitioners	3.68	0.988	0.583
	Pharmacists	3.91	1.003	

There were no statistically significant differences between pharmacists and medical practitioners when it comes to rating the importance of factors that could influence the prescribing of statins (Table 3.19).

Table 3.19: Medical practitioners (N=62) and pharmacists (N=148) mean rating scores when rating the importance of factors that could influence the prescribing of statins to patients with hypercholesterolaemia and/or diabetes mellitus type 2 without previous ASCVD

	Healthcare professional	**Mean rating score**	**Standard deviation**	**p-value**
Indications as per recent guidelines	Medical practitioners	4.53	0.783	0.192
	Pharmacists	4.50	0.733	
Results of recent trials	Medical practitioners	3.84	0.961	0.120
	Pharmacists	3.99	0.896	
Consultation with British National Formulary (BNF)	Medical practitioners	3.48	1.238	0.120
	Pharmacists	3.91	0.824	
Consultation with Summary of Product Characteristics	Medical practitioners	3.61	1.046	0.565
	Pharmacists	4.05	0.852	
Attending specialised courses as part of continuous education	Medical practitioners	3.82	0.984	0.323
	Pharmacists	4.05	0.946	
Consultation with colleagues	Medical practitioners	3.13	1.108	0.866
	Pharmacists	3.63	0.957	
Personal clinical experience	Medical practitioners	3.90	0.844	0.886
	Pharmacists	3.92	0.944	
Pharmacist's recommendation	Medical practitioners	2.82	1.153	0.685
	Pharmacists	3.97	0.860	
Information given by medical representatives	Medical practitioners	2.97	0.991	0.204
	Pharmacists	3.64	1.024	

When comparing the risks associated with prescribing of statins, different comparisons were made. When comparing risk factors of prescribing by medical practitioners, scores given by medical practitioners and by pharmacists were compared and no statistically significant differences were found (Table 3.20). The same was done for pharmacists prescribing. There were no statistically significant differences in scores given by medical practitioners and pharmacists separately for risks associated with statin prescribing by pharmacists (Table 3.21).

Table 3.20: Medical practitioners (N=62) and pharmacists (N=148) mean rating scores when assessing the risks associated with prescribing of statins by medical practitioners

Risk	Healthcare professional	Mean rating score	Standard deviation	p-value
Incomplete medical assessment	Medical practitioners	2.97	1.267	0.637
	Pharmacists	3.50	1.204	
Worsening of patient outcomes	Medical practitioners	2.81	1.212	0.263
	Pharmacists	3.32	1.108	
Under/over treatment	Medical practitioners	3.37	1.105	0.145
	Pharmacists	3.68	1.082	
Incorrect dose of statin	Medical practitioners	3.05	1.179	0.760
	Pharmacists	3.53	1.115	
Wrong choice of statin	Medical practitioners	2.84	1.231	0.114
	Pharmacists	3.59	1.030	
Increased incidence of interactions	Medical practitioners	3.29	1.384	0.158
	Pharmacists	3.81	0.936	
Increased incidence of side-effects	Medical practitioners	3.35	1.307	0.888
	Pharmacists	3.84	0.953	
Incomplete medication review	Medical practitioners	3.05	1.260	0.338
	Pharmacists	3.86	1.024	
Inadequate patient follow-up	Medical practitioners	3.10	1.364	0.623
	Pharmacists	4.05	0.985	
Low patient compliance	Medical practitioners	3.34	1.241	0.858
	Pharmacists	3.73	1.034	
Poor patient satisfaction	Medical practitioners	3.11	1.202	0.532
	Pharmacists	3.32	1.005	
Reduced patient access to medicines	Medical practitioners	2.77	1.323	0.265
	Pharmacists	2.97	1.133	
Increased financial burden on healthcare system	Medical practitioners	2.63	1.218	0.960
	Pharmacists	3.23	1.196	

Table 3.21: Medical practitioners (N=62) and pharmacists (N=148) mean rating scores when assessing the risks associated with prescribing of statins by pharmacists

Risk	Healthcare professional	Mean rating score	Standard deviation	p-value
Incomplete medical assessment	Medical practitioners	4.42	0.984	0.642
	Pharmacists	3.78	1.104	
Worsening of patient outcomes	Medical practitioners	3.42	1.208	0.636
	Pharmacists	2.81	1.090	
Under/over treatment	Medical practitioners	3.68	1.142	0.768
	Pharmacists	3.10	1.147	
Incorrect dose of statin	Medical practitioners	3.11	1.332	0.989
	Pharmacists	2.62	1.223	
Wrong choice of statin	Medical practitioners	3.10	1.238	0.886
	Pharmacists	2.80	1.221	
Increased incidence of interactions	Medical practitioners	2.81	1.316	0.202
	Pharmacists	2.44	1.126	
Increased incidence of side-effects	Medical practitioners	2.94	1.226	0.603
	Pharmacists	2.51	1.110	
Incomplete medication review	Medical practitioners	3.68	1.388	0.692
	Pharmacists	2.98	1.368	
Inadequate patient follow-up	Medical practitioners	4.16	1.190	0.730
	Pharmacists	3.15	1.387	
Low patient compliance	Medical practitioners	3.19	1.143	0.450
	Pharmacists	2.72	1.229	
Poor patient satisfaction	Medical practitioners	3.19	1.212	0.720
	Pharmacists	2.59	1.130	
Reduced patient access to medicines	Medical practitioners	2.58	1.337	0.501
	Pharmacists	2.22	1.232	
Increased financial burden on healthcare system	Medical practitioners	2.79	1.381	0.849
	Pharmacists	2.22	1.222	

Mean rating scores of **risk factors** were compared when medical practitioners prescribed and when pharmacists prescribed. Mean rating scores of the **total** number of healthcare professionals were observed (in total, 210 medical practitioners and pharmacists) (Table 3.22). Two hundred and ten (210) healthcare professionals rated the risk factors for medical practitioners and 210 healthcare professionals rated the risk factors for pharmacists and those scores were compared. No statistically significant differences were found amongst mean rating scores.

Table 3.22: Medical practitioners and pharmacists (observed together, N=210) mean rating scores when assessing the risks associated with prescribing of statins by medical practitioners and by pharmacists

Risk	Healthcare professional who prescribe	Mean rating score	Standard deviation	p-value
Incomplete medical assessment	Medical practitioners	3.34	1.239	0.422
	Pharmacists	3.97	1.106	
Worsening of patient outcomes	Medical practitioners	3.17	1.156	0.790
	Pharmacists	2.98	1.152	
Under/over treatment	Medical practitioners	3.58	1.091	0.370
	Pharmacists	3.27	1.173	
Incorrect dose of statin	Medical practitioners	3.38	1.149	0.141
	Pharmacists	2.94	1.252	
Wrong choice of statin	Medical practitioners	3.36	1.231	0.066
	Pharmacists	2.89	1.138	
Increased incidence of interactions	Medical practitioners	3.65	1.106	0.366
	Pharmacists	2.55	1.194	
Increased incidence of side-effects	Medical practitioners	3.70	1.086	0.960
	Pharmacists	2.64	1.158	
Incomplete medication review	Medical practitioners	3.61	1.153	0.992
	Pharmacists	3.18	1.407	
Inadequate patient follow-up	Medical practitioners	3.76	1.186	0.836
	Pharmacists	3.45	1.407	
Low patient compliance	Medical practitioners	3.61	1.107	0.352
	Pharmacists	2.86	1.221	
Poor patient satisfaction	Medical practitioners	3.25	1.065	0.147
	Pharmacists	2.76	1.188	
Reduced patient access to medicines	Medical practitioners	2.90	1.186	0.946
	Pharmacists	2.31	1.272	
Increased financial burden on healthcare system	Medical practitioners	3.04	1.225	0.418
	Pharmacists	2.39	1.294	

Total risk scores when medical practitioners prescribed and when pharmacists prescribed were compared (Table 3.23). Scores were assessed from the total number of healthcare professionals (both medical practitioners and pharmacists, total 210). There was no statistically significant difference between them (p=0.126). There were no statistically significant differences when **total risk scores** for each group were rated separately by medical practitioners and by pharmacists (p=0.687 and p=0.077 respectively) (Table 3.24).

*Table 3.23: Medical practitioners and pharmacists (observed together, N=210) mean rating scores when assessing the **total risk** associated with prescribing of statins by medical practitioners and by pharmacists*

Total risk of prescribing statins by:	Mean rating score of total risk	Standard deviation	p-value
Medical practitioners	3.41	0.816	0.126
Pharmacists	2.94	0.920	

*Table 3.24: **Total risk** associated with prescribing of statins by medical practitioners and by pharmacists, by opinion of both medical practitioners (N=62) and pharmacists (N=148)*

Healthcare professional who will prescribe	Healthcare professional	Mean rating score of total risk	Standard deviation	p-value
Medical practitioners	Medical practitioners	3.05	0.961	0.687
	Pharmacists	3.56	0.698	
Pharmacists	Medical practitioners	3.30	0.920	0.077
	Pharmacists	2.78	0.878	

Each group of healthcare professionals, when assessing the risks, estimated higher risk scores for the opposite group (pharmacists estimated higher risk score for the medical practitioners, than for the pharmacists and vice versa) (Table 3.25). However, there were no statistically significant differences amongst these scores (p=0.250 and p=0.142).

*Table 3.25: Medical practitioners (N=62) and pharmacists (N=148) mean rating scores when assessing the **total risk** associated with prescribing of statins by medical practitioners and by pharmacists*

Healthcare professional	Healthcare professional who will prescribe	Mean rating score of total risk	Standard deviation	p-value
Medical practitioners	Medical practitioners	3.05	0.961	0.250
	Pharmacists	3.30	0.920	
Pharmacists	Medical practitioners	3.56	0.698	0.142
	Pharmacists	2.78	0.878	

Agreement with recent guideline recommendations was compared between medical practitioners and pharmacists (Table 3.26). Values 1 and 2 were regarded as ‘disagreement’, value 3 as ‘neutral opinion’ and values 4 and 5 were considered as ‘agreement’.

Table 3.26: Agreement of medical practitioners (N=62) and pharmacists (N=148) with specific recommendations regarding prescribing of statins

	Healthcare professional	**Disagreement** **Values 1 and 2** **n (%)**	**Neutral opinion** **Value 3** **n (%)**	**Agreement** **Values 4 and 5** **n (%)**	**p-value**
All patients with diabetes mellitus type 2, aged 40-75 years should be on a statin regardless of their LDL-C levels	Medical practitioners	10 (16.1)	6 (9.7)	46 (74.2)	**0.002**
	Pharmacists	39 (26.4)	37 (25)	72 (48.6)	
All patients with elevated LDL-C, aged 40-75 years should receive a statin, regardless of their CVD risk	Medical practitioners	23 (37.1)	16 (25.8)	23 (37.1)	**0.001**
	Pharmacists	25 (16.9)	31 (20.9)	92 (62.2)	
It is not important which statin is prescribed to patients with chronic kidney disease (CKD)	Medical practitioners	42 (67.7)	12 (19.4)	8 (12.9)	0.370
	Pharmacists	114 (77)	21 (14.2)	13 (8.8)	
If transaminase levels are increased less than three times the upper limit of normal, statin should be discontinued	Medical practitioners	35 (56.4)	12 (19.4)	15 (24.2)	**0.006**
	Pharmacists	49 (33.1)	49 (33.1)	50 (33.8)	
Routine monitoring of creatine kinase levels (as a sign of myopathy) is necessary even in asymptomatic patients	Medical practitioners	36 (58.1)	9 (14.5)	17 (27.4)	**<0.001**
	Pharmacists	28 (18.9)	31 (20.9)	89 (60.2)	
In patients with history of myopathy, statins are contraindicated	Medical practitioners	15 (24.2)	13 (21)	34 (54.8)	0.342
	Pharmacists	28 (18.9)	45 (30.4)	75 (50.7)	
There is a lack of beneficial effect of statins when used for primary prevention in patients aged 40-75 years with hypercholesterolaemia and/or diabetes mellitus type 2	Medical practitioners	53 (85.5)	6 (9.7)	3 (4.8)	**0.002**
	Pharmacists	90 (60.8)	37 (25)	21 (14.2)	
Statins should not be prescribed to patients who have at least one drug which interacts with statins (example, amlodipine)	Medical practitioners	37 (59.7)	18 (29)	7 (11.3)	**0.033**
	Pharmacists	61 (41.2)	53 (35.8)	34 (23)	
Detailed explanation to patient why statin is prescribed, can improve outcomes	Medical practitioners	2 (3.2)	3 (4.8)	57 (92)	0.507
	Pharmacists	10 (6.8)	10 (6.8)	128 (86.4)	
An educational training programme on prescribing of statins is required	Medical practitioners	9 (14.5)	17 (27.4)	36 (58.1)	**0.006**
	Pharmacists	8 (5.4)	23 (15.5)	117 (79.1)	

There was no statistically significant difference in mean rating scores of pharmacist's competence to prescribe statins, when rated by medical practitioners and pharmacists (Table 3.27).

Table 3.27: Medical practitioners (N=62) and pharmacists (N=148) mean rating scores when assessing the pharmacists' competence to prescribe statins

Healthcare professional	Pharmacists' competence to prescribe statins	p-value
Medical practitioners	2.87	0.672
Pharmacists	3.44	

There was a statistically significant difference between pharmacists and medical practitioners support towards giving statin prescribing rights to pharmacists ($p<0.001$) (Table 3.28).

Table 3.28: Medical practitioners (N=62) and pharmacists (N=148) agreement with giving statin prescribing rights to pharmacists

Healthcare professional	In favour of giving prescribing rights of statins to pharmacists	p-value
Medical practitioners	32.3%	**<0.001**
Pharmacists	83.1%	

Table 3.29 represents the factors that could ease the implementation of pharmacist prescribing in Malta as rated by both medical practitioners and pharmacists. The factors 'community pharmacy setting needs to guarantee patient privacy and confidentiality' and 'good collaboration with medical practitioners is vital' deemed as the most important and were assigned the mean rating score of 4.66 out of a maximum of 5. Healthcare professionals thought that the factor '24-hour pharmacy service should be available in Malta' is the least important and it was assigned a mean rating score of 3.18.

Table 3.29: Factors that could promote a smooth implementation of pharmacist prescribing in Malta (N=210)

Factors that promote a smooth implementation of pharmacist prescribing in Malta	Importance score	Standard deviation
Community pharmacy setting needs to guarantee patient privacy and confidentiality	4.66	0.675
Good collaboration with medical practitioners is vital	4.66	0.639
Continuing professional development by pharmacists is essential	4.56	0.788
The programme of pharmacist education at the University of Malta needs to address study units aimed towards pharmacist prescribing	4.54	0.949
Management and other team members in community pharmacies/hospitals need to be supportive and organised, so pharmacists have the time to perform prescribing	4.50	0.898
Specialised training courses for pharmacists to undertake additional prescribing role need to be organised	4.45	1.044
Access to electronic medical records needs to be given to pharmacists	4.36	1.171
A structured system should be in place to facilitate routine follow-up of patients by pharmacists for outcomes (example, pharmacists ordering blood tests)	4.31	1.181
Pharmacist prescribing needs to be recognised as a positive contributor to patient management from all healthcare professionals	4.28	1.062
Pharmacist prescribers need to be adequately remunerated	4.26	1.072
The medical condition needs to be diagnosed by a medical practitioner	4.07	1.096
The prescribing and dispensing roles of pharmacists need to be separated so conflict of interest can be avoided	3.83	1.322
Clinical supervision by a medical practitioner is crucial	3.71	1.224
24-hour pharmacy service should be available in Malta	3.18	1.488

$X^2(13) = 438.843$, $p<0.001$

3.5 Risk Factors Clustering

Cluster analysis was performed for 13 risk factors using assigned risk scores from 420 responses. There was in total 210 healthcare professionals who rated risks of statin prescribing twice, risks of statin prescribing by medical practitioners and risks of statin prescribing by pharmacists.

The TwoStep model summary showed that the optimum number of clusters was 3 with fair quality regarding distribution amongst clusters (Figure 3.21).

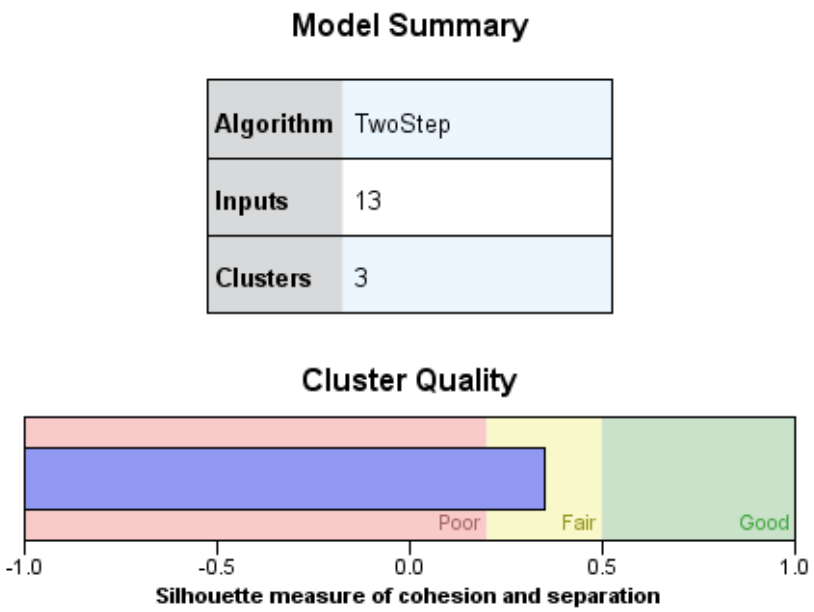


Figure 3.21: Output from TwoStep cluster analysis

Cluster analysis of assigned risk scores was then performed using K-means clustering with 3 clusters (Table 3.30).

Table 3.30: Final cluster centers

Risk factors	Cluster		
	1	2	3
Incomplete medical assessment	2.96	4.39	3.68
Worsening of patient outcomes	1.96	4.22	3.12
Under/over treatment	2.27	4.53	3.53
Incorrect dose of statin	1.97	4.41	3.20
Wrong choice of statin	1.83	4.45	3.19
Increased incidence of interactions	1.77	4.48	3.16
Increased incidence of side-effects	1.80	4.52	3.26
Incomplete medication review	1.94	4.51	3.65
Inadequate patient follow-up	2.06	4.60	3.94
Low patient compliance	2.08	4.25	3.36
Poor patient satisfaction	1.94	3.97	3.13
Reduced patient access to medicines	1.52	3.84	2.61
Increased financial burden on healthcare system	1.61	3.97	2.72

Clusters 1, 2 and 3 represent the different levels of perceived risks associated with prescribing of statins, both by medical practitioners and pharmacists. Healthcare professionals tended to assess the risk factors either as low-risk (cluster 1), moderate-risk (cluster 3) and high-risk (cluster 2). Most participants (n=215, 51.2%) rated the prescribing of statins as a moderate-risk activity (Table 3.31).

Table 3.31: Number of cases in each cluster

Cluster	Risk associated with prescribing of statins	Number of cases
1	Low-risk	109
2	High-risk	96
3	Moderate-risk	215
		Total: 420

When comparing the distribution of cases amongst clusters using TwoStep and K-means clustering methods, it was observed that 9 (2.1%) cases were allocated to different clusters. For the majority of the cases (n=411, 97.9%), allocation into clusters was the same, in both methods used (Table 3.32).

Table 3.32: Distribution of cases amongst clusters using different methods

		K-means cluster number		
		1	**2**	**3**
TwoStep cluster number	**1**	109	0	2
	2	0	91	1
	3	1	5	211

3.6 Regression Models

Two regression analyses were performed.

Regression model I had the aim to predict the total risk associated with statin prescribing. Predictors were risk factors associated with statin prescribing and the healthcare professional responsible for prescription.

In regression model II the aim was to examine the relationship between the chosen predictors and the total risk of statin prescribing, both by medical practitioners and pharmacists.

3.6.1 Regression Model I

ANCOVA regression analysis was used because all the variables were categorical, while the dependant variable was continuous.

The aim was to examine the relationship amongst ‘risk factors’ and ‘Total risk’. Initially 13 ‘risk factors’ were included. When medical practitioners and pharmacists were asked to rate the risk factors, ‘reduced patient access to medicines’ and ‘increased financial burden on healthcare system’ were assigned the lowest risk scores (Figure 3.22). These two risk factors were not included in regression analysis. ‘Worsening of patient outcomes’, which refers to both efficacy and safety outcomes and thus overlaps with ‘incomplete medical assessment’, ‘under/over treatment’, ‘increased incidence of interactions’, increased incidence of side-effects’, ‘incomplete medication review’, ‘inadequate patient follow-up’, ‘low patient compliance’ and ‘poor patient satisfaction’ was excluded. All of these risk factors can, in different ways, lead to worsening of outcomes, either efficacy (patient is exposed to low concentration of statin) or safety (patient is exposed to high concentration of statin). Risk factors ‘incorrect dose of statin’ and ‘wrong choice of statin’ were overlapping with ‘under/over treatment’, so they were excluded. In the final model, 8 risk factors were included.

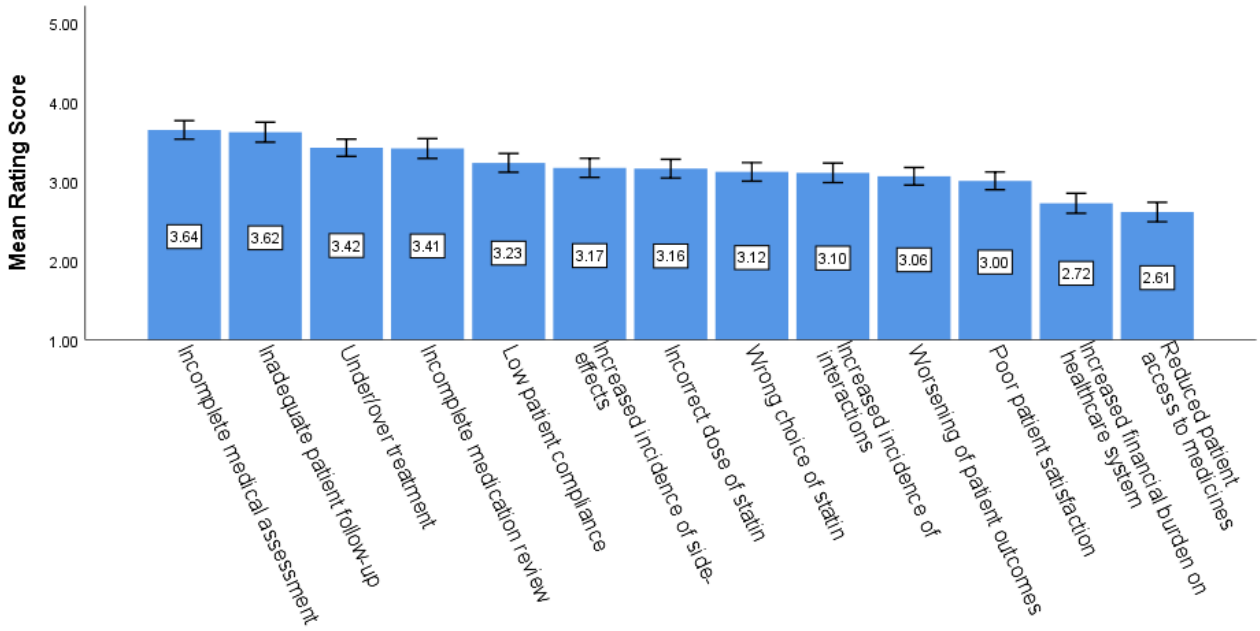


Figure 3.22: Medical practitioners and pharmacists (N=210) mean rating scores when assessing the risks associated with prescribing of statins by medical practitioners and by pharmacists

'Total risk' was calculated as mean of all risk scores associated with healthcare professional's opinion. For regression model I, all 420 answers were included.

Results of regression model I can be found in Table 3.33 and Table 3.34.

Table 3.33: Tests of between-subjects effects, Regression Model I

Source	Sum of Squares	df	Mean Square	F	p-value
Intercept	43.407	1	43.407	31.211	**<0.001**
R_1= Incomplete medical assessment	4.254	1	4.254	19.912	**<0.001**
R_2= Under/over treatment	7.937	1	7.937	37.157	**<0.001**
R_3= Increased incidence of interactions	1.030	1	1.030	4.821	**0.029**
R_4= Increased incidence of side-effects	3.667	1	3.667	17.166	**<0.001**
R_5= Incomplete medication review	5.796	1	5.796	27.133	**<0.001**
R_6= Inadequate patient follow-up	3.035	2	1.518	7.105	**0.001**
R_7= Low patient compliance	1.264	1	1.264	5.916	**0.015**
R_8= Poor patient satisfaction	6.371	2	3.186	14.912	**<0.001**
HCP	0.469	1	0.469	2.195	0.139
Error	87.157	408			

HCP-healthcare professional, which refers to medical practitioner or pharmacist who prescribe statin

Table 3.34: Parameter estimates, Regression Model I

Parameter=Risk factor (R)	B	Standard deviation	p-value
Intercept	1.250	0.070	**<0.001**
R_1= Incomplete medical assessment	0.318	0.071	**<0.001**
R_2= Under/over treatment	0.424	0.070	**<0.001**
R_3= Increased incidence of interactions	0.183	0.083	**0.029**
R_4= Increased incidence of side-effects	0.376	0.091	**<0.001**
R_5= Incomplete medication review	0.374	0.072	**<0.001**
R_6= Inadequate patient follow-up	0.297	0.080	**<0.001**
R_7= Low patient compliance	0.181	0.074	**0.015**
R_8= Poor patient satisfaction	0.360	0.069	**<0.001**
HCP= medical practitioner	0.078	0.053	0.139
HCP= pharmacist*	0	/	/

*HCP=pharmacist was set to zero because it is redundant.

According to results the final model can be written as:

$R = 1.250 + 0.318*R_1 + 0.424*R_2 + 0.183*R_3 + 0.376*R_4 + 0.374*R_5 + 0.297*R_6 + 0.181*R_7 + 0.360*R_8 + 0.078*HCP$

Where:

R=Total risk

R_1= Incomplete medical assessment

R_2= Under/over treatment

R_3= Increased incidence of interactions

R_4= Increased incidence of side-effects

R_5= Incomplete medication review

R_6= Inadequate patient follow-up

R_7= Low patient compliance

R_8= Poor patient satisfaction

HCP= Healthcare professional

All the risk factors can have a value of 0 (not present) or 1 (present), which depends on the individual patient receiving the statin and his/her characteristics. HCP can have value 0 or 1 (0-pharmacist is prescribing and 1-medical practitioner is prescribing).

All the risk factors were statistically significant contributors meaning they significantly contribute to the model. The model is showing that there is no statistically significant

difference (p=0.139) in risks associated with prescribing of statins by medical practitioners and by pharmacists. All the interactions amongst predictors were not statistically significant, therefore they were not included in the final model.

Adjusted R squared is 73.7% which means that the given model explains 73.7% of all variations in the data.

Homogeneity and normality assumptions of the data were satisfied.

Studentized deleted residuals showed 25 outliers. Since a sample have 420 answers, outliers present 6%. All outliners were kept in the model.

3.6.2 Regression Model II

Regression analysis ANCOVA was used to estimate the relationship between predictors, which were all categorical, and dependant variable, which was continuous. The dependant variable was 'Total risk' and predictors were: participant (medical practitioner or pharmacist) who estimated the risks by completing the questionnaire, years of participant's professional experience, the number of patients with hypercholesterolaemia and diabetes mellitus type 2 who the participant encounters on weekly basis, participant's support towards giving of statin prescribing rights to pharmacists and whether participant routinely collaborates with medical practitioners or pharmacists. All 420 responses were included in the final analysis.

Results of regression model II can be found in Table 3.35 and Table 3.36.

Table 3.35: Tests of between-subjects effects, Regression Model II

Source	Sum of Squares	df	Mean Square	F	p-value
Intercept	1701.740	1	1701.740	623.490	0.020
Years of professional experience	5.628	4	1.407	1745	0.139
Number of patients with diabetes mellitus type 2 per week	1.965	3	0.655	0.812	0.488
Number of patients with hypercholesterolaemia per week	2.961	3	0.987	1.225	0.300
Agreement with giving statin prescribing rights to pharmacists	3.814	1	3.814	4.732	**0.030**
Collaboration with other HCP	0.042	1	0.042	0.052	0.819
HCP who estimate the risk	1.298	1	1.298	1.610	0.205

Table 3.36: Parameter estimates, Regression Model II

Parameter		B	Standard deviation	p-value
Intercept		3.076	0.155	<0.001
Years of professional experience	<2 years	-0.066	0.169	0.697
	2-5 years	0.126	0.133	0.345
	6-10 years	-0.230	0.142	0.106
	11-20 years	-0.174	0.134	0.195
	>20 years*	0	/	/
Number of patients with diabetes mellitus type 2 per week	<10	-0.253	0.354	0.475
	10-30	-0.399	0.292	0.173
	31-50	-0.391	0.289	0.176
	>50*	0	/	/
Number of patients with hypercholesterolaemia per week	<10	0.409	0.351	0.244
	10-30	0.513	0.285	0.073
	31-50	0.497	0.274	0.071
	>50*	0	/	/
Attitude towards giving of statin prescribing rights to pharmacists	No	0.243	0.112	**0.030**
	Yes*	0	/	/
Collaboration with other healthcare professional	No	0.022	0.097	0.819
	Yes*	0	/	/
HCP who estimates the risk	Medical practitioner	-0.156	0.123	0.205
	Pharmacist*	0	/	/

*Some parameters were set to zero because they are redundant.

From the results of regression analysis it can be observed that the only statistically significant predictor of 'Total risk' was healthcare professional agreement with giving of statin prescribing rights to pharmacists. There is positive regression coefficient (B=0.243) calculated for the answer 'No' which shows that 'Total risk' would be increased by 0.243 points if the healthcare professional was against giving the statin prescribing rights to pharmacists.

All the interactions amongst predictors were not statistically significant, therefore they were not included in the final model. Homogeneity and normality assumptions of the data were satisfied.

Studentized deleted residuals showed 17 outliers. Since a sample have 420 answers, outliers present 4%. All outliners were kept in the model.

Chapter 4

Discussion

The final analysis of the data from both SPQ_{MedPr} and SPQ_{Pharm} was performed and presented. Cluster analysis was carried out and two regression models were developed.

4.1 Prescribing by Medical Practitioners and Pharmacists: A Local Perspective

When asked to rate the importance of the factors which influence prescribing of statins, medical practitioners and pharmacists rated 'indications as per recent guidelines' and 'contraindications' as the factors of the highest importance, respectively, which is in accordance with Schumock et al (2004). The BNF was not deemed as an important resource, which contrasts results from Attard Pizzuto (2016), where it was found that the BNF was the most consulted source by medical practitioners prior to prescribing. 'Personal clinical experience' was rated similarly by both medical practitioners and pharmacists. This is in agreement with results from studies by Almond & Walley (2003), Schumock et al (2004) and Davari et al (2018), where it was shown that GPs rely on their own clinical experience when prescribing. Possible explanation is that medical practitioners may be more confident using the drugs they usually prescribe because they are familiar with their efficacy and safety profiles.

'Information given by medical representatives' was rated by both professions as one of the least important factors which influence on prescribing, 2.97 by medical practitioners and 3.64 by pharmacists. This is in contrast with studies which reported that GPs rely a lot on information given by the pharmaceutical industry (Almond & Walley, 2003; Davari et al, 2018). Results in this study are supported by Schumock et al (2004) where both

medical practitioners and pharmacists rated influence of pharmaceutical companies on prescribing as low.

While 'CV risk factors', 'LDL-C levels', 'blood glucose', 'liver enzymes levels', 'family history', 'prior response to statin' were all rated as important and very important, it should be noted that 'hypothyroidism', 'gender' and 'patient preference and/or acceptability' were all rated as the least important of all factors (ratings below 4). This is in contrast with Lum et al (2018) who reported that patients' preferences and expectations had a great influence on GP prescribing. Other studies reported that GPs take into consideration patient's preferences (Van Buul et al, 2014; Ju et al, 2018) and that 43% of primary care providers said that they often, very often or always prescribe in accordance to patient preferences (Clough et al, 2019). One of the possible explanations why hypothyroidism and gender were deemed the least important as factors that could influence prescribing of statins, is that they are not portrayed and highlighted in guidelines (Grundy et al, 2019; Mach et al, 2020), when compared to other factors, such as CV risk factors and LDL-C levels. Hypothyroidism should not be underestimated as a possible secondary cause of hypercholesterolaemia, and need to be managed prior to prescribing statins (Grundy et al, 2019; BNF, 2020). In addition, hypothyroidism can increase muscle-related side-effects (Vodnala et al, 2012; BNF, 2020). The influence of gender on prescribing of statins is of relevance because statins should be avoided in pregnancy and be discontinued three months before attempting to conceive, as congenital anomalies have been reported (BNF, 2020).

Both 'cost of the drug' and 'drug inclusion in National Formulary' were rated as the least important factors prior to statin prescribing, by both healthcare professionals. In a study by Schumock et al (2004) medical practitioners said that the cost of a drug has low influence, in contrast to the perception of clinical pharmacists. One possible explanation

of this result in the present study is that in Malta out-of-pocket spending is among the highest in EU, more than twice an EU average and that medications are the second largest portion of total out-of-pocket spending.[25] Simvastatin, atorvastatin and rosuvastatin can be found on the Hospital Formulary List and Out-Patients Formulary List and patients can get them free of charge.

When asked how frequently should lipids be monitored for patients with hypercholesterolaemia and who are on statins, 50% of medical practitioners and 48% of pharmacists participating in this study chose six months, which is in accordance with the current recommendations. Lipid profile should be checked at 6-8 weeks after statin initiation and then after 6-12 months (Mach et al, 2020). Grundy et al (2019) suggest an initial check-up after 4-12 weeks and after that, on every 3-12 months.

Regarding liver function monitoring, both the American Heart Association and the American College of Cardiology (Grundy et al, 2019) and the European Society of Cardiology (Mach et al, 2020) do not recommend routine liver function monitoring, rather checking when there are symptoms of hepatotoxicity. The BNF (2020), although stating that there is some evidence regarding liver function monitoring, is giving its recommendation that monitoring should be performed after 3 months and then after 12 months upon initiation of treatment, with the recommendation being based on NICE guideline from 2014. Out of 210 interviewed medical practitioners and pharmacists in this study, none has chosen the option 'there is no need for liver function monitoring'. This is one of the reasons why frequent educational programmes are needed, to inform healthcare professionals about the most recent recommendations and options available.

25. Organisation for Economic Co-operation and Development (OECD). Malta: Country Health Profile 2019, State of Health in the EU [Internet]. Paris: OECD; 2019 [cited 2021 Mar 15]. Available from URL: https://www.oecd-ilibrary.org/docserver/05db1284-en.pdf?expires=1606919236&id=id&accname=guest&checksum=81B347FCE9573B9E06125F8B958CF7E5

When analysing the responses on the different statements regarding statin treatment, it was observed that medical practitioners were more familiar with guideline recommendations than pharmacists, for the following statements: 'all patients with diabetes mellitus type 2, aged 40-75 years should be on a statin regardless of their LDL-C levels' ($p=0.002$), 'all patients with elevated LDL-C, aged 40-75 years should receive a statin, regardless of their CVD risk' ($p=0.001$), 'if transaminase levels are increased less than three times the upper limit of normal, statin should be discontinued' ($p=0.006$), 'routine monitoring of creatine kinase levels (as a sign of myopathy) is necessary even in asymptomatic patients' ($p<0.001$), 'there is a lack of beneficial effect of statins when used for primary prevention in patients aged 40-75 years with hypercholesterolaemia and/or diabetes mellitus type 2' ($p=0.002$), 'statins should not be prescribed to patients who have at least one drug which interacts with statins (example, amlodipine)' ($p=0.033$). These recommendations are based on the American Heart Association and the American College of Cardiology guideline on the management of blood cholesterol from 2018 (Grundy et al, 2019) and American Diabetes Association, Standards of Medical Care in Diabetes from 2018.[32] Medical practitioners may be more knowledgeable about the recommendations by recent guidelines since they prescribe statins, order blood tests and perform follow-up of patients and thus consult guidelines more. These findings are in contrast with results from the local study by Aquilina et al (2018), where medical practitioners and pharmacists prescribed similar treatment for patients with diabetes mellitus and hypertension and patients on oral anticoagulation therapy.

32.American Diabetes Association. Diabetes Care. Standards of medical care in diabetes – 2018 [Internet]. Arlington, VA: American Diabetes Association; 2018;41(1) [cited 2021 Mar 15]. Available from URL: https://diabetesed.net/wp-content/uploads/2017/12/2018-ADA-Standards-of-Care.pdf

Healthcare professionals are aware of the usefulness of continuous education and according to results of this study, educational training programmes should be organised on the statin prescribing for primary prevention to patients with hypercholesterolaemia and/or diabetes mellitus type 2, for both medical practitioners and pharmacists.

Pharmacists supported giving statin prescribing rights to pharmacists in Malta (83.1%), similarly to other studies done locally (Wirth et al, 2011; Vella et al, 2014; Attard Pizzuto, 2016; Aquilina et al, 2018, Micallef, 2019). Both pharmacists and medical practitioners with less or equal to 20 years of experience thought that pharmacists are more competent to prescribe when compared to those with more than 20 years of experience. A statistically significant difference was observed in pharmacists group ($p=0.038$). Pharmacists are gaining more rights to prescribe (Stone et al, 2020) and evidence about benefits of this activity is increasing (Tsuyuki et al, 2016a; Tsuyuki et al, 2016b; Weeks et al, 2016; Brunisholz et al, 2018; Mills et al, 2018; Derington et al, 2019; Sanyal et al, 2019). Younger generations are more exposed to this evidence during their education and probably that is why their support toward pharmacist prescribing is higher. Older generations can sometimes be averse to change and since they worked with a fixed attitude for more than 20 years, it can be difficult for some to comprehend the reasons or to find a way to change. That is why benefits of prescribing should be clearly presented to experienced healthcare professionals and they should be aware of countries that implemented pharmacist prescribing successfully and of the models used. More experienced healthcare professionals have the skills and are highly trained, and thus are valuable and can significantly contribute to the implementation of pharmacist prescribing.

Similar to findings in this study, pharmacists in other international studies were in favour of expanding their role to prescribing, but they thought that they need more training prior to this activity (George et al, 2006; Auta et al, 2018; Jebara et al, 2018). Other studies

reported some additional benefits of prescribing, such as increased job satisfaction (George et al, 2006; Hill et al, 2014; Bourne et al, 2016, Noblet et al, 2017; Jebara et al 2018; Mills et al, 2020), better self-confidence (George et al, 2006; Hill et al, 2014), increased recognition of pharmacist role in a healthcare team (Attard Pizzuto, 2016), personal growth and enhanced safety of prescribing (Bourne et al, 2016), increased scope of practice (Bourne et al, 2016; Rodriguez et al, 2018; Eckhaus et al, 2021), improved patient care, better access to medicines and reduced patient waiting time (Hill et al, 2014; Attard Pizzuto, 2016, Noblet et al, 2017; Stewart et al, 2017; Jebara et al, 2018; Rodriguez et al, 2018; Rafie et al, 2019; Eckhaus et al, 2021) and better patient satisfaction (George et al, 2006).

Medical practitioners in this study did not support pharmacist prescribing (67.7%). This finding is in agreement with international findings which report disagreement for pharmacist prescribing before the implementation of such a practice. Medical practitioners opposed pharmacist prescribing rights and comprehended the role of clinical pharmacist more as per tradition (Zaidan et al, 2011; Ibrahim & Ibrahim, 2014; Čufar et al, 2014; Attard Pizzuto, 2016; Ahmed et al, 2017; Auta et al, 2018). In a survey from 1990 held in UK, medical practitioners were against pharmacists issuing repeated prescriptions (64%), while 50% thought medical practitioners should be allowed to dispense and 34% agreed that "pharmacists should stick to dispensing and not venture into other areas of medicine" (Spencer & Edwards, 1992). Over time, this negative perception of medical practitioners towards pharmacist prescribing was mostly resolved because medical practitioners had the opportunity to collaborate with pharmacists and observe the outcomes of pharmacist prescribing. With a positive experience from pharmacist prescribers and lack of junior doctors, medical prescribers had a positive perception of this new role of pharmacists in the UK (Bourne et al, 2016). Medical

practitioners who were mentoring pharmacist prescribers in Northern Ireland, were supportive for pharmacist prescribing and trusted pharmacists, believing that they would refer a patient when needed (McCann et al, 2012b). In an addiction clinic in Scotland where pharmacists were able to prescribe, medical practitioners were supportive towards pharmacist prescribing and thought that pharmacists are competent, and that it would be good to have more pharmacist prescribers (Hill et al, 2014). Healthcare professionals who collaborated with the pharmacist independent prescriber in primary care in England were highly supportive of this activity and thought that in this way patient care was improved (Hindi et al, 2019). They trusted the pharmacist independent prescriber and were feeling safe to be patients of pharmacist independent prescribers. They also reported that their respect towards pharmacist independent prescribers increased since the start of their collaboration (Hindi et al, 2019).

Farrell et al (2010) performed a study in Canada which aimed to follow GPs' opinion about pharmacist prescribing during 19 months after the implementation of pharmacist prescriber into GP practice. Pharmacists were educating patients and providing information, performing medication review and performing administrative tasks in the office. In the beginning, GPs had more traditional views regarding pharmacists' scope of practice and thought that pharmacists' contributions were much lower in diagnosis, prescribing and monitoring. As integration of pharmacist prescribers into GP practice was developing and moving forward, GPs' opinion about pharmacists' role changed. They perceived that pharmacists have bigger role in diagnosis and prescribing, medication review and monitoring. Farrell et al (2010) also showed that as GPs were getting trust in the pharmacist and that they were ready to share responsibilities in medication management. The relationship developed over time and GPs' expectations and reliance on pharmacists changed.

In the present study, one of the reasons why pharmacists should not be given prescribing rights, as perceived by all healthcare professionals participating, was lack of access to patient medical records, which is in accordance with findings from other studies (Cooper et al, 2008; Wirth et al, 2011; Attard Pizzuto, 2016; Jebara et al, 2018). Lack of privacy in a community pharmacy setting was also reported as one of the reasons why pharmacists in Malta should not get statin prescribing rights, which is in agreement with Hughes & McCann (2003), Wirth et al (2011) and Attard Pizzuto (2016). Participants from this study were also concerned about pharmacists not being qualified to clinically examine patients, which is in accordance with Hatah et al (2013), Pojskic et al (2014), Attard Pizzuto (2016), Auta et al (2018) and Jebara et al (2018). Other studies reported additional issues where medical practitioners were mostly concerned about patient safety (Cooper et al, 2008; Hatah et al, 2013; Pojskic et al, 2014) and that pharmacists' prescribing would be influenced by commercial interests (Blenkinsopp et al, 2008).

If pharmacists are given prescribing rights, the statements 'medical practitioners will have more time to deal with complex cases' and 'medical practitioners will have more time to expand their services' were supported by pharmacists while medical practitioners had a neutral opinion. These findings were supported by Blenkinsopp et al (2008) where medical practitioners thought that if pharmacists prescribe they could expand their services to specialise or deal with more complex cases. The primary care physician spends around one third of the patient's visit to "treatment planning", both for acute and chronic conditions (Yawn et al, 2003). Pharmacists can help in these drug-related assignments, so medical practitioners have more time to concentrate on other aspects of the visit "for which their training is better suited" (Rose et al, 2017).

In the present study, both pharmacists and medical practitioners disagreed that the professional identity of medical practitioners will be compromised and that medical

practitioner-patient relationship can be jeopardised if pharmacists prescribe. This is in contrary with findings from Blenkinsopp et al (2008), Cooper et al (2008) and Hatah et al (2013). In other studies, medical practitioners saw additional advantages of pharmacist prescribing such as: decreased workload and gaining more time (Blenkinsopp et al, 2008; Hatah et al, 2013, Jebara et al, 2018; Hindi et al, 2019; Lane et al, 2020), enhanced patient care and improved medication review (Hatah et al, 2013) and accessibility to the most recent information about drug-drug interactions and pharmaceutical guidelines (Lane et al, 2020).

Medical practitioners and pharmacists participating in this study thought that medical practitioner-pharmacist collaboration is beneficial for the patient (67.7% and 98% respectively). This opinion was constant, regardless of the years of experience. Medical practitioners who did not routinely collaborate with pharmacists also thought that collaboration is beneficial for the patient. This is a step in the right direction, where potential collaboration with pharmacists is concerned. Pharmacists should be aware of this aspect and should approach medical practitioners offering their services, knowledge and any help regarding patient care.

Pharmacists in this study who do not routinely collaborate with medical practitioners thought that collaboration is beneficial for the patient. Efforts should be made to investigate the reasons why pharmacists do not collaborate with medical practitioners and help them to overcome those barriers. Pharmacists who collaborate routinely with medical practitioners thought that pharmacists are more competent to prescribe statins and were more supportive of giving statin prescribing rights to pharmacists, when compared to those who do not routinely collaborate. A possible explanation can be that pharmacists who routinely collaborate with medical practitioners felt more confident in their knowledge since they had routine communication with the medical practitioner.

Both healthcare professionals reported that the collaboration was limited to whether different generics are available, accessibility on the market and cost. This is in accordance with traditional roles, where medical practitioners are in charge for the prescription and pharmacists are only dispensing the medications.

Healthcare professionals participating in this study were asked to quantify the risks associated with prescribing of statins. Risk quantification enables prioritisation of the risks, application of actions on the risks with the highest ratings (Fischhoff & Morgan, 2011; Langerholc et al, 2018) and enables efficacious communication amongst diverse stakeholders (Langerholc et al, 2018).

In each of the questionnaires, there were two questions which assessed the risks associated with prescribing of statins. The questions dealt with the risks of statin prescribing by medical practitioners and risks of statin prescribing by pharmacists. Both medical practitioners and pharmacists needed to assess the risks when they prescribe and when the other group of healthcare professionals prescribe. Each group estimated that the risk associated with statin prescribing of the other group is higher than their own. Wolff et al (2019) reported that people tend to perceive their own risks differently than risks of others, while Kim et al (2018) specifies that people have the tendency to underemphasise the risk related to themselves. When people think they have control over the specific hazardous situation, they tend to underestimate the risk (Lanciano et al, 2020). Regression model I did not show a statistically significant difference ($p=0.139$) between risks when pharmacists prescribe and risks when medical practitioners prescribe, which is in agreement with Attard Pizzuto (2016) where risks associated with prescribing of antibiotics were assessed.

The risks associated with medical practitioners prescribing were: ‘increased incidence of interactions’ and ‘increased incidence of side-effects’, as perceived by both groups of healthcare professionals. This is in accordance with findings from other studies where pharmacists were seen as experts for medicines (Blenkinsopp et al, 2008; Attard Pizzuto, 2016) and having better pharmacology and drug-drug interactions knowledge (Hatah et al, 2013). The risks associated with pharmacist prescribing were ‘incomplete medical assessment’ and ‘inadequate patient follow-up’, as perceived by both healthcare professionals. This is in agreement with findings from other studies (Hatah et al, 2013; Pojskic et al, 2014; Auta et al, 2018; Jebara et al, 2018) which report concerns regarding pharmacists’ diagnostic and clinical assessment skills. These risks can potentially be reduced if pharmacists were to follow protocols while prescribing statins.

Additional identified risks associated with prescribing of statins, by both medical practitioners and pharmacists, were: under/over treatment, incomplete medication review, low patient compliance, incorrect dose of statin, wrong choice of statin, worsening of patient outcomes, poor patient satisfaction, increased financial burden on healthcare system and reduced patient access to medicines. When ratings of risks were compared between medical practitioners and pharmacists, no statistically significant differences were found. This implies that both healthcare professionals were perceiving the risks of statin prescribing equally.

Assessing risk can be highly subjective (Zhu et al, 2016; Wilson et al, 2019; Benítez-Díaz et al, 2020; Chen et al, 2020; Oh et al, 2020; Lanciano et al, 2020). This is supported with findings from the risk clustering performed in this study, where risks associated with prescribing of statins were grouped according to the values assigned. When assessing the risks, healthcare professionals participating in this study tend to assess the risk factors either as low, moderate or high. The highest number (n=215, 51.2%) of healthcare

professionals rated the risks associated with prescribing of statins, both by medical practitioners and pharmacists, as a moderate-risk activity. A possible explanation can be that participants were not sure how to rate the risk and chose the neutral option. Different perceptions of the risk can influence on different actions taken by person who perceived the risk and thus, changing those perceptions can influence one's behaviour (Aycock et al, 2019). For example, some healthcare professionals upon prescribing statins, will monitor patients more frequently, while some, due to different perceptions of the risks, will schedule an appointment later. Protocols for prescribing of statins to patients with hypercholesterolaemia and/or diabetes mellitus type 2, without previous ASCVD should be used to standardise the treatment and care. Following predefined criteria based on guideline recommendations, pharmacists would provide standardised and seamless care to patients, and the influence of different risk perceptions on practice would be minimised. In this research, validation of the protocols was not done because of the possibility of future changes in guideline recommendations, which would warrant changing of the protocols.

Pharmacists would identify patients at increased risk of worsening of efficacy and safety outcomes and refer the patient to medical practitioners for further evaluations. Using evidence-based recommendations, potential risks associated with prescribing of statins can be prevented or reduced. Protocols for prescribing were helpful in decision making (Stewart et al, 2017) and they enabled pharmacists to safely prescribe and to refer patients when appropriate (Heisler et al, 2012; Akers et al, 2018; Beahm et al, 2018; Klepser & Adams, 2018; Adams, 2020).

With the protocols, risk factors associated with prescribing of statins, as exemplified by, can be significantly reduced:

'Incomplete medical assessment' – patients present to pharmacists either with laboratory results and/or confirmed diagnosis, so as to base the recommendation on objective findings.

'Worsening of patient outcomes' – this risk includes both efficacy and safety outcomes. Detailed instructions to whom statin should be prescribed are ensuring that patients who would have the most benefits from statin treatment are being prescribed statins. By applying exclusion criteria, side-effects of statins are minimised by referring patients with pre-existing risk factors or not eligible for statin treatment, to medical practitioners for further evaluations.

'Under/over treatment' – inclusion/exclusion criteria are ensuring that only those who benefit the most from statin treatment receive the drug.

'Incorrect dose of statin' and 'wrong choice of statin' – special caution should be applied when prescribing to patients with CKD or taking a drug which interacts with statin, so appropriate dose of statin can be prescribed. In some cases, depending of the interacting drug, statins which do not interact can be prescribed. In the case of patients with CKD, guidance from specific summaries of products characteristics regarding appropriate dose can be followed.

'Increased incidence of interactions' – using online interaction checkers can decrease interactions and minimise worsening of outcomes.

'Increased incidence of side-effects' – by referring patients with pre-existing risk factors which make them more susceptible to side-effects, to medical practitioners for further

evaluations, pharmacists are making sure that these patients are assessed additionally and managed accordingly. Prescribing the right dose of statin in case of patients with CKD or with some interacting drug can decrease probability of side-effects.

'Incomplete medication review' – this task remains one of the most demanding tasks for pharmacists and should be approached with high concentration and devotion. Checking the interactions is only one part of this complex process. Healthcare professionals participating in this study, rated this task as fourth highest risk associated with prescribing of statins, with the overall score of 3.41.

'Low patient compliance' and 'poor patient satisfaction' – clear and open communication with the patient and involvement of patient in decision making will increase compliance (Zolnierek & DiMatteo, 2009; Conn & Ruppar, 2017) and improve patient satisfaction (Newnham et al, 2017).

Regression model II showed that agreement with pharmacist prescribing of statins was a statistically significant predictor ($p=0.030$) of total risk associated with prescribing of statins. Those healthcare professionals who were against pharmacists having statin prescribing rights rated the total risk of prescribing higher when compared to those who supported pharmacist prescribing. A possible explanation is that healthcare professionals who perceived the risks associated with prescribing as higher, were concerned for patients' safety if pharmacist prescribe and did not want to support that activity. If the risks associated with prescribing of statins are reduced, support for pharmacist prescribing may increase.

Identified risk factors associated with prescribing of statins can be used to guide regulatory authorities and policy makers in the process of implementation of pharmacist prescribing in Malta. Introducing the protocols for prescribing or prescriptions which

require laboratory results prior to being issued, can increase safety of statin treatment. These actions can be used as instruments to reduce the risks associated with prescribing of statins and thus to increase support towards pharmacist prescribing of statins in Malta.

Risk identification and risk quantification can be applied to other pharmacists' activities, not only prescribing. Dispensing, advising on OTC or dietary supplements, conducting MUR are all activities associated with different risks and will benefit from standardisation. Development of protocols can standardise service provision while reducing risks and promoting patient safety.

When asked about the factors that could ease the implementation of pharmacist prescribing in Malta, both medical practitioners and pharmacists opted for factors which are already well-identified in the literature: appropriate setting in a community pharmacy (Lloyd et al, 2010; Wirth et al, 2011; Attard Pizzuto, 2016; Rafie et al, 2019; Eckhaus et al, 2021), good collaboration with the medical practitioners (Cooper et al, 2008, Lloyd et al, 2010; Makowsky et al, 2013; Attard Pizzuto, 2016; Donald et al, 2017; Stewart et al, 2017; Courtenay et al, 2018; Jebara et al, 2018; Lane et al, 2020), adequate training of the pharmacists (both undergraduate and postgraduate level) (Grindrod et al, 2011; Attard Pizzuto, 2016; Cope et al, 2016; Courtenay et al, 2018; Mody et al, 2019; Rafie et al, 2019; Zhou et al, 2019; Jebara et al, 2020; Mills et al, 2020; Stone et al, 2020; Eckhaus et al, 2021), support of management and other team members (Lloyd et al, 2010; Courtenay et al, 2018; Fisher et al, 2018; Jebara et al, 2018), enough staff and time to prescribe (George et al, 2006; Cooper et al, 2008; Lloyd et al, 2010; Grindrod et al, 2011; Bourne et al, 2016; Stewart et al, 2017; Jebara et al, 2018; Mody et al, 2019; Eckhaus et al, 2021), access to medical records (Cooper et al, 2008; Lloyd et al, 2010; Grindrod et al, 2011; Attard Pizzuto, 2016; Jebara et al, 2018; Mills et al, 2020; Stone et al, 2020), recognition of pharmacists' role by other healthcare professionals, mainly medical

practitioners (George et al, 2006; Hatah et al, 2013; Bourne et al, 2016; Donald et al, 2017; Stewart et al, 2017; Courtenay et al, 2018; Jebara et al, 2018) and adequate reimbursement for pharmacist prescribers (George et al, 2006; Cooper et al, 2008; Lloyd et al, 2010; Hatah et al, 2013; Noblet et al, 2017; Stewart et al, 2017; Courtenay et al, 2018; Jebara et al, 2018; Mody et al, 2019; Smith et al, 2019; Zhou et al, 2019; Mills et al, 2020; Eckhaus et al, 2021).

Participants in the study reported that one of the least important factors for implementation of pharmacist prescribing in Malta was thought to be conflict of interest that might arise if pharmacists were to prescribe and dispense at the same time. Goldacre et al (2019) documented financial influence on prescribing. They showed that GPs who work in dispensing practices in the UK and therefore can have potential financial benefits upon prescribing more expensive drugs, do actually prescribe more expensive drugs, when compared with GPs who do not work in dispensing practices. Although this study was observing the behaviour of GPs, such practices may potentially be extrapolated to community pharmacists if pharmacist prescribing is implemented. The separation of pharmacists' activities while prescribing was also supported by Jebara et al (2020). One way how to overcome this potential conflict of interest is detailed documentation of the pharmacist activity leading to prescribing, explaining all the decisions taken.

Efforts should be made to strengthen the collaboration between medical practitioners and pharmacists due to its numerous benefits (Niquille et al, 2010; Geurts et al, 2012; Hirsch et al, 2014; Morello et al, 2016; Hwang et al, 2017; Rose et al, 2017; Brunisholz et al, 2018; Matzke et al, 2018; Mills et al, 2018; Awdishu et al, 2019). Each healthcare professional is adding into the collaboration unique competences and knowledge (Manolakis & Skelton, 2010). Pharmacists should expand existing collaborations and create new ones which will be based on more active involvement of pharmacists in a

patient care. Pharmacists' knowledge can be used much more efficiently in the healthcare system than just for providing information about availability of the drug and its cost. Pharmacists should not wait for medical practitioners to support their prescribing and to offer them a more active involvement in patient care. Pharmacists should be the initiators and the drivers, to offer their professional services to medical practitioners. Any advice to medical practitioners or to patients, any observed interaction and recommendation for its management will show medical practitioners the value of pharmacists in patient care. Attard Pizzuto (2016) put forward a metaphoric comparison of pharmacists and drivers of a train where pharmacists should lead a campaign to promote pharmacist prescribing to medical practitioners, regulatory authorities and general public. Pharmacists' persistence should guide towards the implementation of pharmacist prescribing (Attard Pizzuto, 2016).

Studies report that, for medical practitioners, trust was highly important for good professional relationship with pharmacists (Löffler et al, 2017) and that trust was based on competence and achievements (Bradley et al 2012; Gregory, 2016). The fact that even medical practitioners and pharmacists participating in this study, who are not part of medical practitioner-pharmacist collaboration think that such collaboration is beneficial for the patient, should be used in order to promote the collaboration and to engage more healthcare professionals. Pharmacists can be the leaders of this change. Pharmacist's personal characteristics can be strong facilitators of collaboration (Jebara et al, 2018). Additional support of regulatory authorities and the academic institutions can significantly influence this change. When benefits of more active involvement of pharmacists in the patient-centred care start to emerge, more healthcare professionals will decide to be part of this kind of collaboration. It will be easier to present and introduce pharmacist prescribing to pharmacists, medical practitioners, general public and

regulatory authorities on the foundation of the system where pharmacists' role in patient-centred care is well-defined and significant.

In literature, different models for strengthening the collaboration were put forward. Gallagher & Gallagher (2012) suggested inter-professional education to be used as early as possible so both groups of healthcare professionals can be aware of skills and competences of each other. Niquille et al (2010) showed that periodical meetings of 3-10 GPs and one trained pharmacist, with the aim of continuous education, can be beneficial. Löffler et al (2017) suggested different engagements where pharmacists can present themselves and their pharmacies to local GPs.

At the same time, continuous education of pharmacists needs to be strengthened and adjusted for the clinical role of pharmacists. Emphasis should be placed on training programmes which will enable working pharmacists to expand their knowledge, to be familiar with the recent recommendations and to regain the confidence in patient-centred care. Results of this study show that pharmacists lack clinical knowledge when it comes to guideline recommendations for statin prescribing. One reason could be that pharmacists do not prescribe themselves and do not order laboratory tests and thus they are not so familiar with guideline recommendations. A possible solution for this could be the setting up of a system where one pharmacist can be solely dedicated to the management of patients, counselling and in the future, prescribing. Having such specialised roles will enable pharmacists to use specific knowledge on daily basis, to be highly skilled in a patient-centred care and to be kept up to date with recent recommendations.

Both medical practitioners and pharmacists participating in this study thought that the community pharmacy setting which will enable patient privacy is highly important for

implementation of pharmacist prescribing. Attard Pizzuto (2016) reported that amongst the participating pharmacists in Malta, 68% said their pharmacy has a private consultation area and 22% stated it has not, but they were willing to adapt it accordingly.

When pharmacists rated the importance of factors which could ease the implementation of pharmacist prescribing in Malta, the two most important factors were providing access to electronic medical records and enabling routine follow-up of patients through ordering of blood tests. Access to patient medical records enabled pharmacists to effectively and safely make an intervention regarding patient drug treatment (Weddle et al, 2017; Hensler et al, 2018). Groppi et al (2018) reported that pharmacists having their own template, as part of electronic medical records where all the interventions were recorded, could help in presenting and tracking the pharmacists' contributions to the healthcare system. Analysis of these achievements can help in more effective organisation of the system. Pharmacists having the access to electronic medical records enables the incorporation of all interventions made by different healthcare professionals for one individual patient (Dreischulte & Guthrie, 2012). In this way, all medical practitioners who are taking care of a patient will be familiar with any changes in the patient's drug treatment made by pharmacists. If pharmacists, while prescribing statins, do not have access to electronic medical records, they should inform all other healthcare professionals involved in the patient's care about the changes made, to ensure the most effective and safe patient management.

When analysing the studies done locally, the public support towards medical practitioner-pharmacist collaboration in the management of chronic conditions improved. Wirth et al (2010) reported that 68% of the interviewed public supported this kind of collaboration, Tabone et al (2013) reported 81% of support, while in the Vella et al (2015) study 93% of the public supported medical practitioner-pharmacist collaboration in management of

chronic conditions. Public support towards pharmacist prescribing changed from 47% (Wirth et al, 2010) and 41% (Tabone et al, 2013) in 2010 and 2013 respectively to 69% in 2015 (Vella et al, 2015). The public agreed 57% (Tabone et al, 2013) and 83% (Vella et al, 2015) that pharmacists should have access to patient medical records.

4.2 Limitations

The low response rate and small sample size are limitations of this research. More participants would make the study sample more representative and would give more applicability to the results. The length of the questionnaire probably contributed to the low response rate.

In the questionnaires, closed-ended questions and questions with Likert scale were used. In these types of questions participants are obliged to choose from offered options, so true attitudes might not be measured. Likert scale can influence participants to answer according to previous answers or to choose answers on one side of the scale (all 1 or all 5). Sometimes, if participants do not understand the question or are unsure of the answer, will choose the neutral option (3). Another limitation is that it could not be ensured that participants were not looking up the answers while filling in the questionnaires. It is not expected from healthcare professionals to know everything by heart, but rather to know where to search for specific information and thus, to provide the best possible healthcare to patients. For this reason, this practice is acceptable while managing patients. However, the possibility that participants were looking up for answers just to fill in the questionnaire while not applying these recommendations in patient management, cannot be ignored. Therefore, the current results might not represent the true situation in the practice.

In this study, recall bias cannot be ignored, since participants filled in the questionnaire according to their memory and their perception. Selection bias might have influenced some of the results of this study. Non-response bias must also be taken into consideration especially because of the low response rate. Participants who did not complete the questionnaires might differ significantly in their views about pharmacist prescribing when compared to those who participated. Therefore, representatives of the sample was not obtained.

Calculating a total response rate was challenging because pharmacists' social media platform also includes students, whose perceptions were not investigated in this study, and one of the medical practitioners' association did not provide a number of members. For these reasons, the total number of pharmacists and medical practitioners to whom questionnaires were distributed electronically was unknown.

This was a study with a cross-sectional design, and a longitudinal design, which would monitor prescribing practices over time, would perhaps be more appropriate and would represent more accurately attitudes and knowledge of healthcare professionals.

In questionnaires used for this study, the prescribing model was not specified and some of the responses and attitudes of the participants may be influenced.

4.3 Recommendations for Further Study

In this research, attitudes of medical practitioners and pharmacists were assessed towards pharmacist prescribing of statins to patients with hypercholesterolaemia and/or diabetes mellitus type 2 without previous ASCVD. Future studies should involve more medical practitioners and pharmacists, so results can be applicable to the real setting. Attitudes

and opinions of the general public towards pharmacist prescribing of statins can be also assessed.

Clough et al (2019) reported that primary care physicians in USA, although they correctly estimated the benefits of statins for primary prevention, had low statin prescription rate. Only 22.3% of eligible patients (out of 6 172) for statin for primary prevention, were prescribed a moderate- or high-intensity statin, in the period 2014-2015 (Clough et al, 2019). One of the future studies can employ a cross-sectional study design, which would determine the percentage of eligible patients for statin treatment, both for primary and secondary care, who are actually on statin treatment. In that way, any gaps in statin treatment of patients in Malta can be addressed.

Other scenarios of pharmacist prescribing can be studied. The prevalence of hypertension in Malta is 36.49% for males and 27.14% for females (Cuschieri et al, 2017) and it was shown that 50.8% of patients on medications did not have controlled hypertension.[33] Pharmacist prescribing for the management of patients with hypertension was already proven to be effective (Green et al, 2008; Carter et al, 2009; Cohen et al, 2011; Franklin et al, 2013; Ip et al, 2013; Magid et al, 2013; Sease et al, 2013; Hirsch et al, 2014; McAlister et al, 2014; Proia et al, 2014; Tsuyuki et al, 2015; Dehmer et al, 2016; Greer et al, 2016; Tsuyuki et al, 2016a; Weeks et al, 2016; Brunisholz et al, 2018; Kennelty et al, 2018; Mills et al, 2018; Victor et al, 2018; Victor et al, 2019) and cost-effective (Dehmer et al, 2016; Marra et al, 2017). Estimation of the risks associated with this kind of prescribing can be undertaken as well as proposition of protocols for pharmacist prescribing for management of hypertension.

33.European Society of Cardiology (ESC). EAPC Country of the month - Malta [internet]. Biot: ESC; 2015 [cited 2021 Mar 15]. Available from URL: https://www.escardio.org/Sub-specialty-communities/European-Association-of-Preventive-Cardiology-(EAPC)/Advocacy/Prevention-in-your-country/Country-of-the-month-Malta

Attitudes of pharmacists and medical practitioners should be assessed towards potential pharmacists' prescribing for hypertension management.

Protocols suggested in this research should be validated prior to be used for the pharmacist prescribing low- and moderate-intensity statins to patients with hypercholesterolaemia and/or diabetes mellitus type 2 without previous ASCVD.

4.4 Conclusion

This research assessed the risks associated with prescribing of statins, both by medical practitioners and pharmacists and the regression model showed that there was no statistically significant difference in risks when any of the two healthcare professionals prescribe. In this study, medical practitioners and pharmacists were equally assessing the risks associated with prescribing of statins.

Pharmacists were supportive regarding pharmacist prescribing of statins, while medical practitioners opposed this practice. Pharmacists who have less or equal to 20 years of experience and those who collaborate with medical practitioners thought that pharmacists are more competent to prescribe, when compared to their more experienced colleagues and those who do not routinely collaborate with medical practitioners. Medical practitioners were more up to date with guideline recommendations regarding statin prescribing than pharmacists.

Those healthcare professionals who were against giving statin prescribing rights to pharmacists gave a higher score for risks associated with statin prescribing. All the actions aiming to reduce the risks associated with statin prescribing, such as protocols, interaction

checkers, prescriptions which cannot be issued without having the blood test, may increase support towards implementation of pharmacist prescribing in Malta. Protocols for pharmacist prescribing of statins to patients with hypercholesterolaemia and/or diabetes mellitus type 2 without previous ASCVD were developed to mitigate the risks associated with this practice.

Factors for potential smooth implementation of pharmacist prescribing in Malta were recommended, such as appropriate setting in a community pharmacy to enable patient privacy, collaboration between medical practitioners and pharmacists, continuous professional development by pharmacists. Efforts should be made to promote and strengthen the collaboration between healthcare professionals in Malta. This research can be helpful to policymakers and stakeholders during the eventuality of pharmacist prescribing in Malta.

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Appendix 1

Questionnaires

University of Malta: Department of Pharmacy

Statin Prescribing Questionnaire for Medical Practitioners

This questionnaire titled "Statin Prescribing Questionnaire for Medical Practitioners" is part of a Doctorate in Pharmacy thesis and is intended for medical practitioners. The questionnaire will take 10-15 minutes to complete. Participation is completely voluntary and all of the responses are anonymous.

This questionnaire will:

i. assess the practices and perceptions related to statin prescribing by medical practitioners,
ii. assess the medical practitioners' opinion about potential pharmacist prescribing of statins,
iii. evaluate medical practitioners' opinion about potential factors which can ease the implementation of pharmacist prescribing in Malta.

For the purpose of this questionnaire, pharmacists will prescribe low- and moderate-intensity statins to patients aged 40-75 years with hypercholesterolaemia and/or diabetes mellitus type 2 for primary prevention of atherosclerotic cardiovascular disease (ASCVD), by following predefined inclusion and exclusion criteria.

Contact details:

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Under the General Data Protection Regulation (GDPR) and national legislation that implements and further specifies the relevant provisions of said Regulation, you have the right to obtain access to, rectify, and where applicable ask for the data concerning them to be erased.

Part ONE

Section I: Demographics

1. How many years have you been practising medicine?

☐ < 2 years
☐ 2-5 years
☐ 6-10 years
☐ 11-20 years
☐ > 20 years

2. Please clarify if you are a:

☐ Foundation Doctor
☐ Basic Specialist Trainee Area of Specialisation: _____
☐ Higher Specialist Trainee Area of Specialisation: _____
☐ Specialist Area of Specialisation: _____
☐ Consultant Area of Practice: _____
☐ Other (please specify): _____

3. **What is the most frequent patient age group that you treat?**

□ ≤ 18 years
□ 19-65 years
□ > 65 years

4. **On average, how many patients do you encounter with hypercholesterolaemia and diabetes mellitus type 2 per week?**

Diabetes mellitus type 2	**Hypercholesterolaemia**
□ < 10	□ < 10
□ 10-30	□ 10-30
□ 31-50	□ 31-50
□ > 50	□ > 50

Section II: Statin prescribing by medical practitioners

5. Rate the importance of the following drug-related information that should be considered when prescribing statins using a scale of 1 to 5.

Drug Information	**Not important at all** →				**Very important**
	1	**2**	**3**	**4**	**5**
Indications as per recent guidelines					
Results of recent trials					
Dosing regimen					
Contraindications					
Precautions					
Monitoring requirements					
Side-effect profile					
Drug-drug interactions					
Cost of the drug					
Drug inclusion in National Formulary					
Other (please specify): _____					

Comments:_____

_____

_____

6. **Rate the importance of the following patient-related information that should be considered when prescribing statins for patients with *hypercholesterolaemia* without previous ASCVD using a scale of 1 to 5.**

Patient Information	**Not important at all** → **1**	**2**	**3**	**4**	**Very important** → **5**
Age					
Gender					
Cardiovascular (CV) risk factors					
LDL-C levels					
Liver enzymes levels					
Renal function					
Hypothyroidism					
Prior response to statin					
Family history					
Patient preference and/or acceptability					
Other (please specify): _____					

Comments:_____

_____

_____

7. **Rate the importance of the following patient-related information to be given consideration, when prescribing statins for patients with *diabetes mellitus type 2* without previous ASCVD using a scale of 1 to 5.**

Patient Information	**Not important at all** → **1**	**2**	**3**	**4**	**Very important** → **5**
Age					
Gender					
CV risk factors					
LDL-C levels					
Blood glucose/HbA1c levels					
Liver enzymes levels					
Renal function					
Hypothyroidism					
Prior response to statin					
Family history					
Patient preference and/or acceptability					
Other (please specify): _____					

Comments:_____

_____

_____

8. **When prescribing statins for patients with *hypercholesterolaemia* without previous ASCVD, how often do you monitor patient's lipid-profile?**

☐ Every 6 weeks
☐ Every 3 months
☐ Every 6 months
☐ Yearly
☐ No specific time frame
☐ There is no need for lipid-profile monitoring
☐ Other (please specify): _____

Comments:_____

_____

_____

9. **When prescribing statins for patients with hypercholesterolaemia and/or diabetes mellitus type 2 without previous ASCVD, how often do you monitor patient's liver function?**

☐ Every 6 weeks
☐ Every 3 months
☐ Every 6 months
☐ Yearly
☐ No specific time frame
☐ There is no need for liver function monitoring
☐ Other (please specify): _____

Comments:_____

_____

_____

10. Rate the importance of the following factors that could influence your prescribing of statins to patients with hypercholesterolaemia and/or diabetes mellitus type 2 without previous ASCVD, using a scale of 1 to 5.

	Not important at all →				**Very important**
	1	**2**	**3**	**4**	**5**
Indications as per recent guidelines					
Results of recent trials					
Consultation with British National Formulary (BNF)					
Consultation with Summary of Product Characteristics					
Attending specialised courses as part of continuous medical education					
Consultation with colleagues					
Personal clinical experience					
Pharmacist's recommendation					
Information given by medical representatives					
Other (please specify): _____					

Comments:_____

_____

_____

11. What risks do you associate with prescribing of statins *by medical practitioners* to patients with hypercholesterolaemia and/or diabetes mellitus type 2 without previous ASCVD?

	Low risk →				**High risk**
	1	**2**	**3**	**4**	**5**
Incomplete medical assessment					
Worsening of patient outcomes					
Under/over treatment					
Incorrect dose of statin					
Wrong choice of statin					
Increased incidence of interactions					
Increased incidence of side-effects					
Incomplete medication review					
Inadequate patient follow-up					
Low patient compliance					
Poor patient satisfaction					
Reduced patient access to medicines					
Increased financial burden on healthcare system					
Other (please specify): _____					

Comments:_____

_____

_____

12. Rate the following statements according to your degree of agreement of 1 to 5.

	Strongly disagree →				**Strongly agree** →
	1	**2**	**3**	**4**	**5**
All patients with diabetes mellitus type 2, aged 40-75 years should be on a statin regardless of their LDL-C levels					
All patients with elevated LDL-C, aged 40-75 years should receive a statin, regardless of their CVD risk					
It is not important which statin is prescribed to patients with chronic kidney disease (CKD)					
If transaminase levels are increased less than three times the upper limit of normal, statin should be discontinued					
Routine monitoring of creatine kinase levels (as a sign of myopathy) is necessary even in asymptomatic patients					
In patients with history of myopathy, statins are contraindicated					
There is a lack of beneficial effect of statins when used for primary prevention in patients aged 40-75 years with hypercholesterolaemia and/or diabetes mellitus type 2					
Statins should not be prescribed to patients who have at least one drug which interacts with statins (example, amlodipine)					
Detailed explanation to patient why statin is prescribed, can improve outcomes					
An educational training programme on prescribing of statins is required					

Comments:_____

_____

_____

Section III: Statin Prescribing by Pharmacists

For the purpose of this study, pharmacists will prescribe low- and moderate-intensity statins to patients aged 40-75 years with hypercholesterolemia and/or diabetes mellitus type 2 for primary prevention of ASCVD, by following predefined inclusion and exclusion criteria. Patients will either present their laboratory results with elevated cholesterol levels or will have a diagnosis of diabetes mellitus type 2. If the pharmacist cannot confirm the patient's diagnosis and/or the signs/symptoms are severe, or if pharmacists have any uncertainty, the pharmacist will refer the patient to a medical practitioner.

13. How would you rate pharmacists' competence to prescribe statins to patients with hypercholesterolaemia and/or diabetes mellitus type 2 without previous ASCVD using a scale of 1 to 5?

Not competent at all				Highly competent
→	→	→	→	→
1	2	3	4	5

In case of a 1 or 2 rating, please state reason(s):

_____

_____

_____

Comments:_____

_____

_____

14. What risks do you associate with prescribing of statins *by pharmacists*, to patients with hypercholesterolaemia and/or diabetes mellitus type 2 without previous ASCVD, if prescribing rights are given to pharmacists in Malta?

	Low risk →				**High risk**
	1	**2**	**3**	**4**	**5**
Incomplete medical assessment					
Worsening of patient outcomes					
Under/over treatment					
Incorrect dose of statin					
Wrong choice of statin					
Increased incidence of interactions					
Increased incidence of side-effects					
Incomplete medication review					
Inadequate patient follow-up					
Low patient compliance					
Poor patient satisfaction					
Reduced patient access to medicines					
Increased financial burden on healthcare system					
Other (please specify): _____					

Comments:_____

_____

_____

15. Do you agree that pharmacists in Malta should be given prescribing rights to start prescribing statins like in other countries, such as United Kingdom, United States of America, Canada and New Zealand[1,2,3,4]?

☐ Yes

☐ No

Comments:_____

_____

_____

1. Royal Pharmaceutical Society of Great Britain. Clinical governance framework for pharmacist prescribers and organisations commissioning or participating in pharmacist prescribing (GB wide) [Internet]. London: Royal Pharmaceutical Society of Great Britain; 2005 [cited 2019 Apr 30]. Available from URL: https://www.palliativedrugs.com/download/clincgovframeworkpharm.pdf
2. National Alliance of State Pharmacy Associations (NASPA). Pharmacist statewide protocols and prescriptive authority [Internet]. North Chesterfield, VA: NASPA; 2018 [cited 2019 Apr 30]. Available from URL: https://naspa.us/resource/swp/#unique-identifier-statewide
3. Canadian Pharmacist Association. Pharmacists' Expanded Scope of Practice [Internet]. Ottawa: Canadian Pharmacist Association; 2018 [cited 2019 Apr 30]. Available from URL: https://www.pharmacists.ca/pharmacy-in-canada/scope-of-practice-canada/
4. New Zealand Ministry of Health. Pharmacist prescriber [Internet]. Wellington: New Zealand Ministry of Health; 2017 [cited 2019 Apr 30]. Available from URL: https://www.health.govt.nz/our-work/health-workforce/new-roles-and-initiatives/established-initiatives/pharmacist-prescriber

16. **Rate the following statements why pharmacists in Malta should *not* be given statin prescribing rights like pharmacists in other countries, using a scale of 1 to 5.**

	Strongly disagree → **1**	**2**	**3**	**4**	**Strongly agree** → **5**
Pharmacists in Malta do not have adequate knowledge and training despite their 5 or 5 and a half year course					
Pharmacists in Malta are not qualified to clinically examine patients					
Pharmacists in Malta are less competent and have less knowledge than pharmacists in other countries who can prescribe					
Pharmacists in Malta cannot order blood tests to monitor patient outcomes					
Pharmacists in Malta do not have access to patient medical records					
Community pharmacies in Malta lack privacy. Confidentiality of the patient data might be endangered because of possible improper communication between the pharmacist and the patient.					
24-hour pharmacy service not available in Malta					
In Malta, there is not enough collaboration between pharmacists and medical practitioners					
Other (please specify): _____					

Comments:_____

_____

_____

17. **If pharmacists are given right to prescribe statins, express your level of agreement with the following statements using a scale of 1 to 5?**

	Strongly disagree →				**Strongly agree**
	1	**2**	**3**	**4**	**5**
Medical practitioners will experience a lower number of patients and will be affected financially					
Medical practitioners will have more time to deal with complex cases					
Medical practitioners will have more time to expand their services					
Professional identity of medical practitioners will be compromised					
Medical practitioner-patient relationship can be jeopardised					

Comments:_____

_____

_____

Section IV: Medical practitioner–Pharmacist Collaboration

18. **How much is the medical practitioner-pharmacist collaboration beneficial for the patient?**

Not beneficial at all →				**Very beneficial**
1	**2**	**3**	**4**	**5**

Comments:_____

_____

_____

19. Do you routinely collaborate with a pharmacist in your medical practice?

☐ Yes *(go to question 20, skip question 21)*

☐ No *(go to question 21, skip question 20)*

Comments:_____

_____

_____

20. Before prescribing statins, how often do you consult a pharmacist in order to discuss the following issues, using a scale of 1 to 5?

	Never →				**Always**
	1	**2**	**3**	**4**	**5**
Choice of statin considering patient's history and current medical conditions					
Dosing regimen					
Side-effect profile					
Drug-drug interactions					
Availability on the market					
Availability of different brands of the active ingredient/Generics					
Cost of the drug					
Other (please specify): _____					

Comments:_____

_____

_____

21. Are you willing to start collaborating with a pharmacist?

- ☐ Yes
- ☐ No

If the answer is NO, please state reason(s):

_____

_____

_____

Comments:_____

_____

_____

Part TWO

Rate the importance of the following factors that promote a smooth implementation of pharmacist prescribing in Malta. Please use numbers 1 to 5 (1 is *not important at all* and 5 is *very important*).

Factors that promote a smooth implementation of pharmacist prescribing in Malta	**Importance**
The programme of pharmacist education at the University of Malta needs to address study units aimed towards pharmacist prescribing	
Specialized training courses for pharmacists to undertake additional prescribing role need to be organised	
Continuing professional development by pharmacists is essential	
The medical condition needs to be diagnosed by a medical practitioner	
Clinical supervision by a medical practitioner is crucial	
Good collaboration with medical practitioners is vital	
Community pharmacy setting needs to guarantee patient privacy and confidentiality	
Management and other team members in community pharmacies/hospitals need to be supportive and organised, so pharmacists have the time to perform prescribing	
The prescribing and dispensing roles of pharmacists need to be separated so conflict of interest can be avoided	
Access to electronic medical records needs to be given to pharmacists	
A structured system should be in place to facilitate routine follow-up of patients by pharmacists for outcomes (example, pharmacists ordering blood tests)	
Pharmacist prescribing needs to be recognised as a positive contributor to patient management from all healthcare professionals	
Pharmacist prescribers need to be adequately remunerated	
24-hour pharmacy service should be available in Malta	

Comments:_____

_____

_____

Thank you very much for taking the time to complete this questionnaire.

University of Malta: Department of Pharmacy

Statin Prescribing Questionnaire for Pharmacists

This questionnaire titled "Statin Prescribing Questionnaire for Pharmacists" is part of a Doctorate in Pharmacy thesis and is intended for pharmacists. The questionnaire will take 10-15 minutes to complete. Participation is completely voluntary and all of the responses are anonymous.

This questionnaire will:

i. assess pharmacists' awareness related to statin prescribing,
ii. assess the pharmacists' opinion about potential pharmacist prescribing of statins,
iii. evaluate pharmacists' opinion about potential factors which can ease the implementation of pharmacist prescribing in Malta.

For the purpose of this questionnaire, pharmacists will prescribe low- and moderate-intensity statins to patients aged 40-75 years with hypercholesterolaemia and/or diabetes mellitus type 2 for primary prevention of atherosclerotic cardiovascular disease (ASCVD), by following predefined inclusion and exclusion criteria.

Contact details:

Milica Jovanovic

Email: milica.jovanovic.17@um.edu.mt

Mobile: 77 89 43 62

Under the General Data Protection Regulation (GDPR) and national legislation that implements and further specifies the relevant provisions of said Regulation, you have the right to obtain access to, rectify, and where applicable ask for the data concerning them to be erased.

Part ONE

Section I: Demographics

1. **How many years have you been practising pharmacy?**

□ < 2 years
□ 2-5 years
□ 6-10 years
□ 11-20 years
□ > 20 years

2. **Please clarify if you work in a:**

□ Community pharmacy
□ Hospital
□ Academia
□ Regulatory sciences
□ Pharmaceutical industry
□ Pharmaceutical company
□ Other (please specify): _____

3. **What is the most frequent patient age group that you come into contact with?**

☐ ≤ 18 years
☐ 19-65 years
☐ > 65 years

4. **On average, how many patients do you encounter with hypercholesterolaemia and diabetes mellitus type 2 per week?**

Diabetes mellitus type 2	**Hypercholesterolaemia**
☐ < 10	☐ < 10
☐ 10-30	☐ 10-30
☐ 31-50	☐ 31-50
☐ > 50	☐ > 50

Section II: Statin prescribing

5. **Rate the importance of the following drug-related information that should be considered when statins are prescribed using a scale of 1 to 5.**

Drug Information	**Not important at all** →				**Very important**
	1	**2**	**3**	**4**	**5**
Indications as per recent guidelines					
Results of recent trials					
Dosing regimen					
Contraindications					
Precautions					
Monitoring requirements					
Side-effect profile					
Drug-drug interactions					
Cost of the drug					
Drug inclusion in National Formulary					
Other (please specify): _____					

Comments:_____

_____

_____

6. **Rate the importance of the following patient-related information that should be considered when statins are prescribed for patients with *hypercholesterolaemia* without previous ASCVD using a scale of 1 to 5.**

Patient Information	**Not important at all** → **1**	**2**	**3**	**4**	**Very important** → **5**
Age					
Gender					
Cardiovascular (CV) risk factors					
LDL-C levels					
Liver enzymes levels					
Renal function					
Hypothyroidism					
Prior response to statin					
Family history					
Patient preference and/or acceptability					
Other (please specify): _____					

Comments:_____

_____

_____

7. **Rate the importance of the following patient-related information to be given consideration, when statins are prescribed for patients with *diabetes mellitus type 2* without previous ASCVD using a scale of 1 to 5.**

Patient Information	**Not important at all** →				**Very important**
	1	**2**	**3**	**4**	**5**
Age					
Gender					
CV risk factors					
LDL-C levels					
Blood glucose/HbA1c levels					
Liver enzymes levels					
Renal function					
Hypothyroidism					
Prior response to statin					
Family history					
Patient preference and/or acceptability					
Other (please specify): _____					

Comments:_____

_____

_____

8. **When statins are prescribed for patients with *hypercholesterolaemia* without previous ASCVD, how often should a patient's lipid-profile be monitored?**

☐ Every 6 weeks
☐ Every 3 months
☐ Every 6 months
☐ Yearly
☐ No specific time frame
☐ There is no need for lipid-profile monitoring
☐ Other (please specify): _____

Comments:_____

_____

9. **When statins are prescribed for patients with hypercholesterolaemia and/or diabetes mellitus type 2 without previous ASCVD, how often should patient's liver function be monitored?**

☐ Every 6 weeks
☐ Every 3 months
☐ Every 6 months
☐ Yearly
☐ No specific time frame
☐ There is no need for liver function monitoring
☐ Other (please specify): _____

Comments:_____

_____

10. Rate the importance of the following factors that could influence the prescribing of statins to patients with hypercholesterolaemia and/or diabetes mellitus type 2 without previous ASCVD, using a scale of 1 to 5.

	Not important at all →				**Very important**
	1	**2**	**3**	**4**	**5**
Indications as per recent guidelines					
Results of recent trials					
Consultation with British National Formulary (BNF)					
Consultation with Summary of Product Characteristics					
Attending specialised courses as part of continuous education					
Consultation with colleagues					
Personal clinical experience					
Pharmacist's recommendation					
Information given by medical representatives					
Other (please specify): _____					

Comments:_____

_____

_____

11. What risks do you associate with prescribing of statins *by medical practitioners* to patients with hypercholesterolaemia and/or diabetes mellitus type 2 without previous ASCVD?

	Low risk →				**High risk**
	1	**2**	**3**	**4**	**5**
Incomplete medical assessment					
Worsening of patient outcomes					
Under/over treatment					
Incorrect dose of statin					
Wrong choice of statin					
Increased incidence of interactions					
Increased incidence of side-effects					
Incomplete medication review					
Inadequate patient follow-up					
Low patient compliance					
Poor patient satisfaction					
Reduced patient access to medicines					
Increased financial burden on healthcare system					
Other (please specify): _____					

Comments:_____

_____

_____

12. Rate the following statements according to your degree of agreement of 1 to 5.

	Strongly disagree → **1**	**2**	**3**	**4**	**Strongly agree** → **5**
All patients with diabetes mellitus type 2, aged 40-75 years should be on a statin regardless of their LDL-C levels					
All patients with elevated LDL-C, aged 40-75 years should receive a statin, regardless of their CVD risk					
It is not important which statin is prescribed to patients with chronic kidney disease (CKD)					
If transaminase levels are increased less than three times the upper limit of normal, statin should be discontinued					
Routine monitoring of creatine kinase levels (as a sign of myopathy) is necessary even in asymptomatic patients					
In patients with history of myopathy, statins are contraindicated					
There is a lack of beneficial effect of statins when used for primary prevention in patients aged 40-75 years with hypercholesterolaemia and/or diabetes mellitus type 2					
Statins should not be prescribed to patients who have at least one drug which interacts with statins (example, amlodipine)					
Detailed explanation to patient why statin is prescribed, can improve outcomes					
An educational training programme on prescribing of statins is required					

Comments:_____

_____

_____

Section III: Statin Prescribing by Pharmacists

For the purpose of this study, pharmacists will prescribe low- and moderate-intensity statins to patients aged 40-75 years with hypercholesterolemia and/or diabetes mellitus type 2 for primary prevention of ASCVD, by following predefined inclusion and exclusion criteria. Patients will either present their laboratory results with elevated cholesterol levels or will have a diagnosis of diabetes mellitus type 2. If the pharmacist cannot confirm the patient's diagnosis and/or the signs/symptoms are severe, or if pharmacists have any uncertainty, the pharmacist will refer the patient to a medical practitioner.

13. How would you rate the pharmacists' competence to prescribe statins to patients with hypercholesterolaemia and/or diabetes mellitus type 2, without previous ASCVD using a scale of 1 to 5?

Not competent at all				Highly competent
1	2	3	4	5

In case of a 1 or 2 rating, please state reason(s):

_____

_____

_____

Comments:_____

_____

_____

14. What risks do you associate with prescribing of statins *by pharmacists*, to patients with hypercholesterolaemia and/or diabetes mellitus type 2 without previous ASCVD, if prescribing rights are given to pharmacists in Malta?

	Low risk →				**High risk**
	1	**2**	**3**	**4**	**5**
Incomplete medical assessment					
Worsening of patient outcomes					
Under/over treatment					
Incorrect dose of statin					
Wrong choice of statin					
Increased incidence of interactions					
Increased incidence of side-effects					
Incomplete medication review					
Inadequate patient follow-up					
Low patient compliance					
Poor patient satisfaction					
Reduced patient access to medicines					
Increased financial burden on healthcare system					
Other (please specify): _____					

Comments:_____

_____

_____

15. Do you agree that pharmacists in Malta should be given prescribing rights to start prescribing statins like in other countries, such as United Kingdom, United States of America, Canada and New Zealand[1,2,3,4]?

☐ Yes

☐ No

Comments:_____

_____

_____

1. Royal Pharmaceutical Society of Great Britain. Clinical governance framework for pharmacist prescribers and organisations commissioning or participating in pharmacist prescribing (GB wide) [Internet]. London: Royal Pharmaceutical Society of Great Britain; 2005 [cited 2019 Apr 30]. Available from URL: https://www.palliativedrugs.com/download/clincgovframeworkpharm.pdf
2. National Alliance of State Pharmacy Associations (NASPA). Pharmacist statewide protocols and prescriptive authority [Internet]. North Chesterfield, VA: NASPA; 2018 [cited 2019 Apr 30]. Available from URL: https://naspa.us/resource/swp/#unique-identifier-statewide
3. Canadian Pharmacist Association. Pharmacists' Expanded Scope of Practice [Internet]. Ottawa: Canadian Pharmacist Association; 2018 [cited 2019 Apr 30]. Available from URL: https://www.pharmacists.ca/pharmacy-in-canada/scope-of-practice-canada/
4. New Zealand Ministry of Health. Pharmacist prescriber [Internet]. Wellington: New Zealand Ministry of Health; 2017 [cited 2019 Apr 30]. Available from URL: https://www.health.govt.nz/our-work/health-workforce/new-roles-and-initiatives/established-initiatives/pharmacist-prescriber

16. **Rate the following statements why pharmacists in Malta should *not* be given statin prescribing rights like pharmacists in other countries, using a scale of 1 to 5.**

	Strongly disagree → 1	2	3	4	**Strongly agree** → 5
Pharmacists in Malta do not have adequate knowledge and training despite their 5 or 5 and a half year course					
Pharmacists in Malta are not qualified to clinically examine patients					
Pharmacists in Malta are less competent and have less knowledge than pharmacists in other countries who can prescribe					
Pharmacists in Malta cannot order blood tests to monitor patient outcomes					
Pharmacists in Malta do not have access to patient medical records					
Community pharmacies in Malta lack privacy. Confidentiality of the patient data might be endangered because of possible improper communication between the pharmacist and the patient.					
24-hour pharmacy service not available in Malta					
In Malta, there is not enough collaboration between pharmacists and medical practitioners					
Other (please specify): _____					

Comments:_____

_____

_____

17. **If pharmacists are given rights to prescribe statins, express your level of agreement with the following statements using a scale of 1 to 5?**

	Strongly disagree →				**Strongly agree**
	1	**2**	**3**	**4**	**5**
Medical practitioners will experience a lower number of patients and will be affected financially					
Medical practitioners will have more time to deal with complex cases					
Medical practitioners will have more time to expand their services					
Professional identity of medical practitioners will be compromised					
Medical practitioner-patient relationship can be jeopardised					

Comments:_____

_____

_____

Section IV: Medical practitioner–Pharmacist Collaboration

18. **How much is the medical practitioner-pharmacist collaboration beneficial for the patient?**

Not beneficial at all →				**Very beneficial**
1	**2**	**3**	**4**	**5**

Comments:_____

_____

_____

19. Do you routinely collaborate with a medical practitioner in your daily practice?

☐ Yes *(go to question 20, skip question 21)*

☐ No *(go to question 21, skip question 20)*

Comments:_____

_____

_____

20. How often are you consulted by a medical practitioner before prescribing statins, in order to discuss the following issues, using a scale of 1 to 5?

	Never →				**Always**
	1	**2**	**3**	**4**	**5**
Choice of statin considering patient's history and current medical conditions					
Dosing regimen					
Side-effect profile					
Drug-drug interactions					
Availability on the market					
Availability of different brands of the active ingredient/Generics					
Cost of the drug					
Other (please specify): _____					

Comments:_____

_____

_____

21. Are you willing to start collaborating with a medical practitioner?

- ☐ Yes
- ☐ No

If the answer is NO, please state reason(s):

_____

_____

_____

Comments:_____

_____

_____

Part TWO

Rate the importance of the following factors that promote a smooth implementation of pharmacist prescribing in Malta. Please use numbers 1 to 5 (1 is *not important at all* and 5 is *very important*).

Factors that promote a smooth implementation of pharmacist prescribing in Malta	**Importance**
The programme of pharmacist education at the University of Malta needs to address study units aimed towards pharmacist prescribing	
Specialized training courses for pharmacists to undertake additional prescribing role need to be organised	
Continuing professional development by pharmacists is essential	
The medical condition needs to be diagnosed by a medical practitioner	
Clinical supervision by a medical practitioner is crucial	
Good collaboration with medical practitioners is vital	
Community pharmacy setting needs to guarantee patient privacy and confidentiality	
Management and other team members in community pharmacies/hospitals need to be supportive and organised, so pharmacists have the time to perform prescribing	
The prescribing and dispensing roles of pharmacists need to be separated so conflict of interest can be avoided	
Access to electronic medical records needs to be given to pharmacists	
A structured system should be in place to facilitate routine follow-up of patients by pharmacists for outcomes (example, pharmacists ordering blood tests)	
Pharmacist prescribing needs to be recognised as a positive contributor to patient management from all healthcare professionals	
Pharmacist prescribers need to be adequately remunerated	
24-hour pharmacy service should be available in Malta	

Comments:_____

_____

_____

Thank you very much for taking the time to complete this questionnaire.

Appendix 2

Ethics Approval

L-Università ta' Malta

Faculty of
Medicine & Surgery

University of Malta
Msida MSD 2080, Malta

Tel: +356 2340 1879/1891/1167
umms@um.edu.mt

www.um.edu.mt/ms

Ref No: **FRECMDS_1819_065**

Monday 24th June 2019

Ms Milica Jovanovic
Flat 1,
Triq Salvu Guillaumier 10,
Santa Venera.

Dear Ms Milica Jovanovic,

Please refer to your application submitted to the Research Ethics Committee in connection with your research entitled:

Risk of Pharmacist Prescribing with Statins

The Faculty Research Ethics Committee granted ethical approval for the above mentioned protocol.

Yours sincerely,

Professor Pierre Mallia
Chairman
Research Ethics Committee

Appendix 3

Protocols

The protocols for pharmacists while potentially prescribing low- and moderate-intensity statins to patients with hypercholesterolaemia and/or diabetes mellitus type 2 without previous ASCVD were based on 'Pharmacist Prescriptive Authority Protocol for Statins for Patients with Diabetes'.[1]

Protocol for pharmacists while potentially prescribing low- and moderate-intensity statins to patients with hypercholesterolaemia:

Inclusion criteria

- Patients aged 40-75 years of age and with LDL-C levels ≥1.8mmol/L<4.9mmol/L. Patient needs to have at least 2 laboratory results with elevated lipids taken 1-12 weeks apart.

- Patient's cardiovascular disease (CVD) risk score should be calculated in order to properly assess need for statin treatment. SCORE[2] (Systematic Coronary Risk Estimation) system can be used in order to estimate CVD risk score. Interventions towards reducing of LDL-C levels based on CVD risk score and initial LDL-C levels can be found in Table 1.

1. Idaho State Board of Pharmacy (BOP). Rule Docket 27-0104-1701. Pharmacist Prescriptive Authority Protocol for Statins for Patients with Diabetes. Boise:BOP; 2018.
2. European Association of Preventive Cardiology (EAPC). HeartScore. The interactive tool for predicting and managing the risk of heart attack and stroke [Internet]. Biot: EAPC;2018 [cited 2021 Mar 15]. Available from URL: https://www.heartscore.org/

Exclusion criteria

Patients to whom statin should not be prescribed by pharmacists and/or should be referred to a medical practitioner:

- Patients younger than 40 years and older than 75 years of age;
- Patients with history of ASCVD (myocardial infarction, stable or unstable angina, arterial revascularisation, stroke, transient ischemic attack or peripheral arterial disease), with heart failure with reduced ejection fraction or with diabetes mellitus;
- Patients with history of rhabdomyolysis or myopathy due to a statin;
- Patients on dialysis or haemodialysis;
- Patients with active liver disease and/or transaminase levels more than three times the upper limit of normal;
- Patients with LDL-C levels ≥4.9mmol/L;
- Women of childbearing age, who are pregnant or breastfeeding;
- Patients with known allergy to a statin.

Caution while prescribing:

- Patients with hypothyroidism;
- Patients with CKD levels 1-4;
- Patients with high alcohol intake;
- Patient having one or more drugs which interact with statin.

Before prescribing statin, initial blood results should be available, assessing lipids (LDL-C, HDL, non-HDL, total cholesterol), renal function, liver function, thyroid function and creatine kinase levels, for those at risk for myopathy (patients with family history of muscle symptoms or patients with statin interacting drugs). With these results available, efficacy and safety of the treatment can be monitored and assessed. Lipids should be rechecked after 4-12 weeks after the beginning of treatment and then after every 3 to 12 months (and more often if the dose is changed). Recommended LDL-C treatment targets can be found in Table 2.

Liver function test and creatine kinase levels should not be monitored routinely, but should be rechecked in symptomatic patients. Regular monitoring of HbA1c should be performed at patients with increased risk for diabetes mellitus (elderly, obese, with metabolic syndrome or insulin resistance). Available online tools for checking the interactions should be used, to minimise interactions to happen and both efficacy and safety outcomes to worsen.

Reasons why statin is prescribed should be clearly explained to patients, with all the benefits of its treatment. Side-effects also need to be explained and patients to be instructed what to do in case they suspect on some side-effect. Patients should be involved in treatment decisions regarding introduction of new drug, type and dose of statin. Patients need to feel comfortable to reach the pharmacist in case of any question or if problem arise.

Table 1: Interventions towards reducing of LDL-C levels based on CVD risk score and initial LDL-C levels

Total CV risk score %	LDL-C levels before the treatment		
	1.8 to <2.6 mmol/L	2.6 to <3.0 mmol/L	3.0 to 4.9 mmol/L
<1, low-risk	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding the drug if uncontrolled
≥1 to <5, moderate-risk	Lifestyle advice	Lifestyle intervention, consider adding the drug if uncontrolled	Lifestyle intervention, consider adding the drug if uncontrolled
≥5 to <10, high-risk	Lifestyle intervention, consider adding the drug if uncontrolled	Lifestyle intervention and concomitant drug treatment	Lifestyle intervention and concomitant drug treatment
≥10, or at very-high-risk due to a risk condition	Lifestyle intervention and concomitant drug treatment	Lifestyle intervention and concomitant drug treatment	Lifestyle intervention and concomitant drug treatment
Very-high-risk (secondary prevention)	Lifestyle intervention and concomitant drug treatment	Lifestyle intervention and concomitant drug treatment	Lifestyle intervention and concomitant drug treatment

Adopted from: Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L et al; The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS). 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. European Heart Journal. 2020;41:111188

Table 2: Recommended LDL-C treatment goals

CV risk categories	**Patient characteristics**	**LDL-C treatment goals**
Very-high-risk	eGFR<30 mL/min Patients with familial hypercholesterolaemia and one more risk factor[1] Calculated SCORE ≥10%	<1.4 mmol/L
High-risk	BP ≥ 180/110 mmHg TC > 8 mmol/L Patients with familial hypercholesterolaemia without other risk factors[1] eGFR 30-59 mL/min Calculated SCORE ≥5% and <10%	<1.8 mmol/L
Moderate-risk	Calculated SCORE ≥1% and <5%	<2.6 mmol/L
Low-risk	Calculated SCORE <1%	<3 mmol/L

Adapted from: Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L et al; The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS). 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. European Heart Journal. 2020;41:111188

[1]*Risk factors*: hypertension, age, smoking, obesity, dyslipidaemia

BP-blood pressure, eGFR-estimated glomerular filtration rate, SCORE-systematic coronary risk estimation, TC-total cholesterol

Protocol for pharmacists while potentially prescribing moderate-intensity statins to patient with diabetes mellitus type 2

Inclusion criteria

- Patients eligible for the statin treatment prescribed by pharmacist are those aged 40-75 years of age with previous diagnosis of diabetes mellitus type 2.

Exclusion criteria

Patients to whom statin should not be prescribed by pharmacists and/or should be referred to a medical practitioner:

- Patients younger than 40 years and older than 75 years of age;
- Patients with history of ASCVD (myocardial infarction, stable or unstable angina, arterial revascularisation, stroke, transient ischemic attack or peripheral arterial disease) or with heart failure with reduced ejection fraction;
- Patients with history of rhabdomyolysis or myopathy due to a statin;
- Patients on dialysis or haemodialysis;
- Patients with active liver disease and/or transaminase levels more than three times the upper limit of normal;
- Women of childbearing age, who are pregnant or breastfeeding;
- Patients with known allergy to a statin.

Caution while prescribing:

- Patients with hypothyroidism;

- Patients with CKD levels 1-4;
- Patients with high alcohol intake;
- Patient having one or more drugs which interact with statin.

Before prescribing statin, initial blood results should be available, assessing lipids (LDL, HDL, non-HDL, total cholesterol, triglycerides), renal function, liver function, thyroid function and for those at risk for myopathy (very elderly with comorbidities, patients with family history of muscle symptoms, or patients with interacting drugs), creatine kinase levels. With these results available, it will be easier to monitor and assess the effect and safety of the treatment. Lipids should be checked after 4-12 weeks after the beginning of treatment and then after every 3 to 12 months (and more often if the dose is changed). Recommended LDL-C treatment targets can be found in Table 3.

Liver function test and creatine kinase levels should not be monitored routinely, but should be checked in symptomatic patients. Available online tools for checking the interactions should be used, to minimise interactions to happen and both efficacy and safety outcomes to worsen.

Reasons why statin is prescribed should be clearly explained to patients, with all the benefits of its treatment. Side-effects also need to be explained and patients to be instructed what to do in case they suspect on some side-effect. Patients should be involved in treatment decisions regarding introduction of new drug, type and dose of statin. Patients need to feel comfortable to reach the pharmacist in case of any question or problem arise.

Table 3: Recommended LDL-C treatment goals

CV risk categories	**Patient characteristics**	**LDL-C treatment goals**
Very-high-risk	Patients with diabetes mellitus And target organ damage[1] Or three or more risk factors[2]	<1.4 mmol/L
High-risk	Diabetes mellitus without target organ damage, with duration ≥10 years Or another additional risk factor[2]	<1.8 mmol/L
Moderate-risk	Patients <50 years with duration of diabetes mellitus <10 years, without any risk factors[2]	<2.6 mmol/L

Adapted from: Cosentino F, Grant PJ, Aboyans V, Bailey CJ, Ceriello A, Delgado V et al; The Task Force for diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD). 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. European Heart Journal. 2020; 41:255-323.

[1]*Target organ damage*: eGFR<30 mL/min, proteinuria, retinopathy or left ventricular hypertrophy

[2]*Risk factors*: hypertension, age, smoking, obesity, dyslipidaemia

All patients with diabetes mellitus type 2 aged 40-75 years of age should be on statin treatment, regardless of their initial LDL-C levels is a recommendation from guidelines[3] from USA (Arnett et al, 2019; Grundy et al, 2019). Introduction of statin for primary prevention needs to be assessed on the individual basis for individuals younger than 40 years and older than 75 years of age (Arnett et al, 2019; Grundy et al, 2019).

Patients with LDL-C levels ≥1.8mmol/L<4.9mmol/L aged 40-75 (without diabetes mellitus type 2) should be further assessed for CVD risk and accordingly, statin introduction can be considered (Grundy et al, 2019; Mach et al, 2020) (Table 1). By recommendations of European Society of Cardiology guidelines (Mach et al, 2020) to those with LDL-C levels with <1.8mmol/L, statin is not needed except to those at very-high-risk or for secondary prevention and those patients should be referred to medical practitioner. By Mach et al (2020), those patients with LDL-C levels ≥4.9mmol/L, can be in low-, moderate- or high-risk group. However, considering that they will need reduction of LDL-C levels of at least 40-50%, high-potency statin is needed. By American Heart Association and American College of Cardiology guidelines, to patients who have LDL-C levels ≥4.9mmol/L high-intensity statin should be prescribed (Grundy et al, 2019). Since the proposed framework of pharmacist prescribing is for low- and moderate-intensity statins, these patients should be referred to medical practitioner.

Statins should be avoided in pregnancy or 3 months before attempt to conceive because of reported congenital anomalies (BNF, 2020; Mach et al, 2020).

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3. American Diabetes Association. Diabetes Care. Standards of medical care in diabetes – 2021 [Internet]. Arlington, VA: American Diabetes Association; 2021;44(1) [cited 2021 Mar 15]. Available from URL https://care.diabetesjournals.org/content/diacare/suppl/2020/12/09/44.Supplement_1.DC1/DC_44_S1_final_copyright_stamped.pdf

In patients with history of rhabdomyolysis or myopathy statins are not contraindicated and patients should reach LDL-C goal on maximally tolerated dose of statin (Mach et al, 2020). Patients should be, depending of the increase in CK levels, restarted with the same statin or in some situations with some other potent statin, with alternate dosing (Mach et al, 2020). That is why it is recommended those patients to be referred to medical practitioner for further evaluations and assessments.

In patients on haemodialysis or dialysis statin should not be initiated, when used for primary prevention (Tonelli et al, 2013; Mach et al, 2020).

Patients with transaminase levels more than three times the upper limit of normal or active liver disease, should be assessed for reasons of increased liver function test and if levels persist high, statin should be avoided (BNF, 2020, Mach et al, 2020). Grundy et al (2019) advises for patients who are already taking the statin that decrease in statin dose or alternative statin often reduce liver transaminase levels.

For patients with heart failure, there is no documented value of starting the statin, when used for primary prevention, however continuation of this therapy can be considered in patients already taking statins when developing heart failure (Ponikowski et al, 2016; Lee et al, 2019; Mach et al, 2020).

Pharmacists should pay additional attention to the cases in ‘caution’ section because of the possible interventions. Patients with hypothyroidism need to be assessed additionally to check if the hypothyroidism is controlled. Hypothyroidism can be possible secondary cause of hypercholesterolaemia, so need to be managed prior to prescribing statins (Grundy et al, 2019; BNF, 2020; Mach et al, 2020). In addition, hypothyroidism can increase muscle-related side-effects (Vodnala et al, 2012; BNF, 2020).

Patients with CKD 1-4 or having some drug interacting with statins, need to be additionally assessed by pharmacists because these patients can require lower doses of statins, depending on the case.

High alcohol intake can increase risk for liver function abnormalities (Mach et al, 2020) and muscle-related side effects (BNF, 2020).

Before starting statin treatment assessment of lipids, including LDL, HDL, non-HDL, total cholesterol, triglycerides, liver function (BNF, 2020; Mach et al, 2020), renal and thyroid function should be done (BNF, 2020). In patients with high-risk of muscle related side-effects baseline CK levels should be checked (Mach et al, 2020). Lipid profile should be checked at 4-12 weeks after statin initiation and then after 3-12 months (Grundy et al, 2019; Mach et al, 2020). Initial assessment and regular monitoring of HbA1c should be done in individuals at high-risk of diabetes mellitus, including elderly, obese, those with metabolic syndrome or insulin resistance (BNF, 2020; Mach et al, 2020).

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