Patient-Centred Regulatory Audits in Community Pharmacy

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To my dear parents who sacrificed their all to make this achievement possible.

To my dear fiancé, Daniel, who was ever-present during the hardest of times.

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Abstract

The pharmacy profession is a patient-centred practice, where the pharmacist translates science to regulated practice. Pharmacy practice has evolved from compliance and adherence to concordance. Could regulation adopt the same concept?

The objectives of this research were to: (1) Retrospectively analyse community pharmacy regulatory audit (CPRA) reports, (2) develop, validate and implement an updated tool for CPRAs, and (3) identify and analyse case studies from CPRAs to recommend improvements in patient safety.

The methodology involved: (1) retrospective analysis of CPRA reports to extract features that could lead to identification of patient-related deficiencies in community pharmacy practice, (2) development of an updated audit tool using data from the retrospective analysis and interviews with community pharmacists, (3) validation of the audit tool by eight auditors from the Malta Medicines Authority and two community pharmacists, (4) implementation of the audit tool in routine CPRAs, (5) identifying desirable patient-related improvements through observation, and (6) engaging in informal educational discussions with the practicing pharmacists during CPRAs. Case studies on deficiencies related to patient safety were identified and evaluated. Dossiers, European Public Assessment Reports and consultation with the Marketing Authorisation Holders were sources that provided the background for the case studies analysis.

A total of 512 CPRA reports for a 57-month period (January 2012-September 2016) were analysed. Interviews with 12 community pharmacists were performed extracting 14 patient-focused recommendations. The audit tool was implemented during CPRAs in 85 pharmacies over an 11-month period (January-November 2017). Seven case studies were evaluated and analysed including 4 dispensing problems (errors, near misses, lack of

proper prescription, unsupervised pharmacy staff), 2 inventory deficiencies (expired items, inappropriate storage temperature) and 1 inequity of treatment between private and government-sponsored patients. Concordance with the pharmacist was reached and actions (N=46) with a patient-centred focus were taken to address the identified deficiencies. Standard operating procedures were developed, such as for temperature recording and for referral of patients to the pharmacist for ailments requiring medicines. Methods for alerts were devised and communication with patients, including when a possible error is detected, were identified.

An educational approach by the auditor in CPRAs, reaching concordance to regulation as distinct to forceful compliance, may improve pharmacist motivation and patient care outcomes.

Keywords

Case Studies - Community Pharmacy Regulatory Audit - Concordance - Deficiencies - Educational Approach - Patient Safety

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Glossary

Accompanying Auditor

A person who conducts an audit and accompanies the audit team leader (European Committee for Standardisation, 2015).

Audit

A systematic, independent and documented process for obtaining audit evidence (records, statements of facts or other information) and evaluating it objectively to determine the extent to which the audit criteria are fulfilled (European Committee for Standardisation, 2015).

Audit Criteria

Set of policies, procedures or requirements (Russell, 2013)

Audit Findings

Results from an audit process that indicate either that audit criteria are (conformity) or are not (non-conformity) being met and identify best practices or improvement opportunities (European Committee for Standardisation, 2015)

Audit Plan

Set of one or more audits planned for a specific timeframe and directed towards a specific purpose (European Committee for Standardisation, 2015).

Calibration

Demonstration that a particular instrument or device produces results within specified limits by comparison with those produced by a reference or traceable standard over an appropriate range of measurements (International Conference on Harmonisation, 2000).

Central Procurement and Supplies Unit

Responsible to stock medicines which are listed on the Government Formulary List (Government of Malta, 2017)

Cleaning Records Register

A record for documentation of cleaning activities carried out at the pharmacy premises in order to comply with the standard stipulated in Subsidiary Legislation 458.16 Pharmacy License to ensure that pharmacy premises are kept clean (Ministry for Justice, Culture and Local Government, 2007).

Corrective Action

An action taken to eliminate the cause/s of a non-conformity, defect, or other undesirable situation to prevent recurrence (reactive) (European Committee for Standardisation, 2015).

Daily Register

A record for documentation of the sale of each medicine dispensed against a repeat prescription and a partially dispensed prescription (Ministry for Justice, Culture and Local Government, 2007).

Dangerous Drugs Purchases Register

Also referred to as DDA purchases, is a record for documentation of all dangerous drugs (narcotics and psychotropic drugs) purchased or otherwise obtained by the pharmacy (Ministry for Justice, Culture and Local Government, 1939).

Dangerous Drugs Sales Register

Also referred to as DDA sales, is a record for documentation of all dealings of dangerous drugs (narcotics and psychotropic drugs) in the pharmacy, including sales and supply to persons outside the Maltese Islands (Ministry for Justice, Culture and Local Government, 1939).

Deficiency

An audit finding that does not conform to the audit criteria (European Committee for Standardisation, 2015).

European Public Assessment Report

Set of documents describing the evaluation of a medicine authorised via the centralised procedure and including the product information published on the European Medicines Agency website (European Medicines Agency, 2018a).

Expiration Date

The time interval during which a product is expected to remain within the approved shelf-life specifications, provided that it is stored under the conditions defined on the label in the proposed container-closure system (International Conference on Harmonisation, 2007).

Follow-up Audit

There are two types of follow-up audits. Type a follow-up audits are carried out after submission of a new application, usually following the issue of a 'List of works' to check for compliance. These audits are notified in advance. Type b follow-up audits are carried out to confirm that corrective and preventive actions are implemented following findings during a renewal or spot-check audit. These audits are not notified in advance and an audit tool is used (Malta Medicines Authority, 2018).

Green prescription

A medical prescription for the supply of narcotics and psychotropic drugs (Ministry for Justice, Culture and Local Government, 1939).

Lead Auditor

Person who conducts an audit appointed as the audit team leader (European Committee for Standardisation, 2015).

License Holder

The holder of a pharmacy license, a legal document which authorises an individual or any entity to have a pharmacy in operation (Ministry for Justice, Culture and Local Government, 2004; International Conference on Harmonisation, 2007).

List of Works

A letter issued after a follow-up audit type a consisting of a list of requirements that need to be satisfied for a pharmacy license to be granted. These requirements are in accordance to standards of conditions of a pharmacy license stipulated in the Medicines Act (Ministry for Justice, Culture and Local Government, 2003).

Locum Register

A record kept for documentation of pharmacists, other than the managing pharmacist, engaged to work at a pharmacy (Ministry for Justice, Culture and Local Government, 2007).

Marketing Authorisation Holder

A person or legal entity who has applied and received the right to market and sell a product in a pharmaceutical form or a set of pharmaceutical forms (European Commission, 2004).

New Application Audit

An audit performed when a new application to open a pharmacy is received by the Malta Medicines Authority and an audit follows to issue a 'List of Works' that need to be carried out to ensure that the premises are in accordance with the required standards. This audit is notified in advance (Malta Medicines Authority, 2018).

Pharmacy-Of-Your-Choice scheme

A national pharmaceutical service offered in community pharmacies for patients who are entitled to receive medicines or pharmaceutical devices free-of-charge from the government. These medicines and devices are for chronic conditions and are listed in the Government Formulary List. The patient selects the pharmacy of his/her choice and collects these medicines and devices from the chosen pharmacy, usually every 8 weeks (Ministry for Health, 2017).

Preventive Action

An action taken to eliminate the cause/s of a potential non-conformity, defect, or other undesirable situation to prevent occurrence (proactive) (European Committee for Standardisation, 2015).

Quality Management System

System comprising activities by which an organisation/entity identifies its objectives and determines the processes and resources required to achieve desired results, such as development of standard operating procedures (European Committee for Standardisation, 2015).

Regulatory Authority

A body that carries out regulatory activities relating to medicines, including the processing of marketing authorisations, monitoring of side-effects, audits, quality testing and monitoring the use of medicines. The regulatory authority in Malta is the Malta Medicines Authority (European Medicines Agency, 2018a).

Renewal Audit

An audit carried out every two years according to a pre-set audit plan to be able to renew the pharmacy license issued by the Malta Medicines Authority and is not notified in advance. During this audit, the routine community pharmacy regulatory audit takes place and an audit tool is used (Malta Medicines Authority, 2018).

Spot-Check Audit

An audit carried out following receipt of a complaint from a patient, pharmacist or stakeholder and is not notified in advance. This audit entails the use of an audit tool (Malta Medicines Authority, 2018).

Standard Operating Procedure

Detailed, written instructions to achieve uniformity of the performance of activities. These instructions provide a general framework, enabling the efficient implementation and performance of the functions and activities for a particular process. These procedures are the basis for an effective quality management system (European Commission, 2004).

Summary of Product Characteristics

A document describing the properties and the officially approved conditions of use of a medicine, used as a source of information for healthcare professionals on the safe and effective use of medicines (European Medicines Agency, 2018b).

Temperature Register

A record for documentation of the maximum and minimum refrigerator and ambient temperature in the pharmacy where medicines are stored in order to comply with the standard in Subsidiary Legislation 458.16 Pharmacy License to ensure that all medicines present on the pharmacy premises are protected from the adverse effects of extremes of temperature (Ministry for Justice, Culture and Local Government, 2007).

Variation Audit

An audit carried out following receipt of a variation of an existing pharmacy license, such as a change in location of the pharmacy. Not all variations require an audit since some variations are only administrative, such as a change in the managing pharmacist or a change in the license holder. This audit is notified in advance (Malta Medicines Authority, 2018).

Warning Letter

A letter which may be issued following a renewal, spot-check or follow-up type b audit depending on findings relating to the audit criteria. Pre-set criteria by the Malta Medicines Authority on which a warning letter is issued are; (1) when one of the deficiencies identified during an audit can potentially affect the quality of medicines stored at the pharmacy or its licensed storage site(s), for example incorrect storage temperatures, excessive humidity or presence of mould, or (2) when one of the deficiencies had been identified in previous audits (Malta Medicines Authority, 2016).

References

European Commission (EC). EudraLex - Volume 4 - Good Manufacturing Practice (GMP) guidelines – Glossary [Online]. Brussels: EC; 2004c [cited 2018 May 30]. Available from: URL: https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/pdfs-en/glos4en200408_en.pdf

European Committee for Standardisation (CEN). Quality management systems - Fundamentals and vocabulary (EN ISO 9000:2015). Brussels: CEN; 2015.

European Medicines Agency (EMA). Glossary [Online]. UK: EMA; 2018a [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/ema/index.jsp?curl=pages/document_library/landing/glossary.jsp

European Medicines Agency (EMA). How to prepare and review a summary of product characteristics [Online]. UK: EMA; 2018b [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000357.jsp

European Medicines Agency (EMA). Note for guidance on definitions and standards for expedited reporting [Online]. CPMP/ICH/3945/03 UK: EMA; 2004 [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002807.pdf

Government of Malta. Central Procurement and Supplies Unit [Online]. Malta; Government of Malta: 2017 [cited 2018 May 30]. Available from: URL: http://deputyprimeminister.gov.mt/en/cpsu/Pages/About-Us/Corporate-Identity.aspx

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). Guidelines for submitting application for registration of a medicine [Online]. Geneva: ICH; 2007a [cited 2018 May 30]. Available from: URL: http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Organisation/SADC/Guideline_for_Medicine_Registration.pdf

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). ICH Harmonised Tripartite Guideline – Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients Q7 [Online]. Geneva: ICH; 2000 [cited 2018 May 30]. Available from: URL: https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q7/Step4/Q7_Guideline.pdf

Malta Medicines Authority. Pharmacies [Online]. Malta: Malta Medicines Authority; 2018 [cited 2018 May 30]. Available from: URL: http://medicinesauthority.gov.mt/Pharmacies

Malta Medicines Authority. Standard Operating Procedure IN035: Procedure to be followed before, during and after a pharmacy inspection. Malta; Malta Medicines Authority: 2016.

Ministry for Health. National outpatients' services booklet [Online]. Malta: Pharmacy-Of-Your-Choice; 2017 [cited 2018 May 30]. Available from: URL: https://deputyprimeminister.gov.mt/en/poyc/Documents/National%20Outpatients'%20Services'%20Booklet%201st%20Draft%20ENGLISH%20[for%20website].pdf

Ministry for Justice, Culture and Local Government. Chapter 458 Medicines Act [Online]. Malta: The Ministry; 2003 [cited 2018 May 30]. Available from: URL: http://www.justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=8924&l=1

Ministry for Justice, Culture and Local Government. Subsidiary Legislation 458.16 Pharmacy License Regulations [Online]. Malta: The Ministry; 2007 [cited 2018 May 30]. Available from: URL: http://www.justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=11256&l=1

Ministry for Justice, Culture and Local Government. Subsidiary Legislation 101.02 Internal Control of Dangerous Drugs Rules [Online]. Malta: The Ministry; 1939 [cited 2018 may 30]. Available from: URL: http://www.justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=9261&l=1

Russell J. The ASQ auditing handbook. Milwaukee, Wisconsin.: ASQ Quality Press; 2013.

List of Abbreviations

ADR	Adverse Drug Reaction
CAPA	Corrective Action and Preventive Action
CPRA	Community Pharmacy Regulatory Audit
EPAR	European Public Assessment Report
FIP	International Pharmaceutical Federation
GPP	Good Pharmacy Practice
IED	Inspectorate and Enforcement Directorate
ISO	International Organisation for Standardisation
MAH	Marketing Authorisation Holder
max/min	Maximum and Minimum
MMA	Malta Medicines Authority
POM	Prescription Only Medicine
POYC	Pharmacy-Of-Your-Choice
PPP	Pregnancy Prevention Programme
SOP	Standard Operating Procedure
WHO	World Health Organization

Chapter One

Introduction

> *"One thing all liberal professions [such as lawyers, architects, auditors, doctors and pharmacists] traditionally have in common is a high level of regulation. I would like to stress here the word 'traditionally'. […] It is interesting to note that the most regulated professions are also the oldest ones, such as pharmacists and notaries: these are professions that were established at the time of the guilds! By contrast, newer professions, which could, in theory, aspire to a special status, are not regulated at all. I am thinking for example of computer scientists: the 'engineers' of our paperless society, who hold the keys to the system of many businesses."*[1]

Monti M. 'Competition in Professional Services: New Light and New Challenges' Speech presented for Bundesanwaltskammer in Berlin on 21 March 2003.

This quote was stated by the former European Commissioner for Competition and former Italian technocratic Prime Minister, Mario Monti, during a speech on 'Competition in Professional Services: New Light and New Challenges', in Berlin on 21 March 2003. This quote highlights the high level of regulation that existed from the establishment of the pharmacy profession, in contrast to newer professions with little or no regulation. Liberal professions, including the pharmacy profession, are closely regulated by national governments or professional bodies to safeguard the patient.[2] Community pharmacy activities are regulated by regulatory bodies through regulatory audits.

[1]Monti M. Competition in professional services: New light and new challenges speech [Online] presented for Bundesanwaltskammer in Berlin on 21 March 2003 [cited 2018 May 30]. Available from: URL: http://ec.europa.eu/competition/speeches/text/sp2003_070_en.pdf

[2] European Commission. Liberal professions - Growth [Online]. European Commission Internal Market, Industry, Entrepreneurship and SMEs. 2018 [cited 2018 May 30]. Available from: URL: https://ec.europa.eu/growth/smes/promoting-entrepreneurship/we-work-for/liberal-professions_en

1.1 Evolution of the community pharmacy profession

The pharmacy profession experienced many changes since the middle of the last century, which led to the evolvement of the profession from being mainly product-oriented, towards focusing more on patient-centred care (Azzopardi, 2000; Rapport et al, 2010; Bugnon et al, 2012; Baines, 2014; Awaisu et al 2015; Duffull et al, 2018; Fang et al, 2018).

The pharmacy profession was established in the eighteenth century, whereby the work of druggists and chemists was recognised as pharmacy. In the 1950s, the role of the community pharmacist consisted mainly of compounding magisterial preparations and dispensing medicines (Azzopardi, 2000; Al-Shaqha et al, 2001; Coley, 2004; Duffull et al, 2018). After the Second World War, the pharmaceutical industry emerged and the traditional apothecary role of the community pharmacist did not remain the main activity (Malerba et al, 2015; Duffull et al, 2018). With the development of the pharmaceutical industry, the pharmacy profession shifted considerably from preparing medicines to dispensing industrially-prepared medicines (Al-Shaqha et al, 2001; Coley, 2004; Pearson, 2007; Duffull et al, 2018). Advances in medicine and the expansion of the pharmaceutical market led to increased availability of medicines, prompting more awareness regarding safe and effective drug therapy and of the pharmacist as the pharmacotherapy expert (Shawahna et al, 2017; Duffull et al, 2018).

The concept of 'pharmaceutical care', defined by Hepler and Strand as "the direct, responsible provision of medication-related care for the purpose of achieving definite outcomes that improve a patient's quality of life", emerged in the 1990s. Pharmaceutical

care provision is key to providing professional patient-centred pharmacy services (Hepler et al, 1990; Hepler, 2004). The introduction of the pharmaceutical care concept extended the role of pharmacists to the application of drug knowledge and clinical skills in practice (Al-Shaqha et al, 2001), and resulted in the shift from a product-oriented to a patient-oriented pharmacy profession (Dahiya et al, 2012; Costa et al, 2017; Duffull et al, 2018). Clinical pharmacy is well-established in many hospitals and is progressing in the community setting (Bugnon et al, 2012; Costa et al, 2017; Duffull et al, 2018). Pharmacist manpower is reported as the highest in the community setting and this statistic should encourage further evolvement of the clinical activities of community pharmacists towards more patient-centred interventions to improve patient outcomes (Bates et al, 2016).

The International Pharmaceutical Federation (FIP) conducts a global survey of its member organisations, including Malta, to investigate how the pharmacy profession is practiced, regulated and remunerated, the status of the global pharmacy workforce, and how medicines are distributed to patients worldwide. 'Pharmacy at a Glance 2015-2017' summarises the key findings of this survey and confirms that the core business of pharmacists still remains the distribution of drugs within community pharmacy practice, whereby 75% of actively practicing pharmacists work in community pharmacy, compared to 13% who practice in hospital pharmacy, and 12% in other areas, including the pharmaceutical industry, pharmaceutical wholesaling, clinical biology laboratories, academia and regulatory affairs.[3]

[3] International Pharmaceutical Federation. Pharmacy at a glance 2015-2017 [Online]. The Hague: International Pharmaceutical Federation; 2017 [cited 2018 May 30]. p. 8. Available from: URL: https://fip.org/files/fip/publications/2017-09-Pharmacy_at_a_Glance-2015-2017.pdf

1.2 The community pharmacist in 'modern' health care

The community pharmacist in 'modern' health care dispenses industrially-prepared medicines and provides patient-centred extended services to patients (Rapport et al, 2010; Bugnon et al, 2012; Philipsen, 2014; Baines, 2014; Duffull et al, 2018). Community pharmacists are highly accessible heath care professionals (Kelling, 2015), and their responsibilities have shifted considerably towards the utilisation of pharmaceutical knowledge in the rational use of medicines and towards interventions to ensure that an individual patient's drug therapy is appropriate, effective, safe and convenient (Azzopardi, 2000; Awaisu et al, 2015; Thamby et al, 2014; Duffull et al, 2018).

Nowadays, the extended responsibilities of the community pharmacist focus on patient safety through the provision of pharmaceutical care (Rapport et al, 2010; Bugnon et al, 2012; Philipsen, 2014; Baines, 2014; Duffull et al, 2018). Community pharmacist patient-centred interventions to ensure patient safety include clinical checking of the correct indication and dose, checking for contraindications and potential side-effects, identifying drug therapy problems, and providing pharmacological and non-pharmacological advice (Bugnon et al, 2012; Dahiya et al, 2012; Duffull et al, 2018).

Community pharmacists provide a primary beneficent service in the diagnosis and treatment of minor ailments by recommending non-prescription medicines to patients. The community pharmacist intervenes by analysing the situation on a risk-benefit basis, excluding non-minor ailments, while balancing the possible risk of side-effects versus benefits of the recommended medicine. This risk-benefit analysis in community pharmacy enhances patient safety (Bugnon et al, 2012; Duffull et al, 2018).

In modern health care, the community pharmacist provides patient-centred services to reduce risks of chronic diseases complications, such as through point-of-care blood pressure measurement, blood glucose, HbA1c and cholesterol testing and INR monitoring, in cardiovascular disease and diabetes mellitus (Dahiya et al, 2012; Scicluna et al, 2012; McMullen et al, 2014; Moffit et al, 2014; Melton et al, 2017; Hall et al, 2018). The community pharmacist promotes healthy nutrition and lifestyle practices, has a role in immunisation and support women's health such as through health campaigns. In chronic disease management, the community pharmacist performs medicine use reviews to reduce polypharmacy and drug therapy problems and collaborates with other health care providers in order to provide effective health care to the patient (Dahiya et al, 2012; Scicluna et al, 2012; McMullen et al, 2014; Moffit et al, 2014; Melton et al, 2017; Dufful et al, 2018; Hall et al, 2018).

1.3 Patient-oriented characteristics of the community pharmacist

Pharmacists possess various skills and competences enabling them to assume different roles as effective health care team members (Thamby et al, 2014). A report of a World Health Organisation (WHO) consultative group on the 'Role of the pharmacist: Preparing the future pharmacist', published in 1997, outlines the role of the pharmacist as 'The seven-star pharmacist'.[4] Due to the change in the philosophical aspect of pharmacy practice and the introduction of pharmaceutical care, the Vancouver consultancy agreed that pharmacists must possess specific knowledge, attitudes, skills and behaviours to support their roles.[4]

[4] World Health Organisation. The role of the pharmacist in the health care system [Online]. Geneva: World Health Organisation; 1997 [cited 2018 May 30]. p. 3-4. Available from: URL: http://apps.who.int/medicinedocs/pdf/s2214e/s2214e.pdf

The concept of 'the seven-star pharmacist' (WHO, 1997) specifies seven roles of the pharmacist as a:

(1) **'care-giver',** where the pharmacist provides caring services, interacts with individuals and populations and offers services of high quality. These services can be clinical, analytical, technological or regulatory-related, and the practice of the pharmacist should be integrated and continuous with other pharmacists and health care professionals.

(2) **'decision-maker',** where the foundation of the pharmacist's activities must revolve around accurate decisions taken regarding the appropriate, efficacious and cost-effective use of resources, such as personnel, medicines, chemicals, equipment, procedures and practices. Achieving this goal requires the ability to evaluate, synthesise and decide upon the most appropriate course of action.

(3) **'communicator',** where the pharmacist is in an ideal position to provide a link between the physician and the patient. The pharmacist must be knowledgeable and confident in interacting with the public and other health care professionals. There are different methods of communication, including verbal, non-verbal, listening and writing skills, and the pharmacist must possess effective communication skills to communicate with patients and practitioners in the provision of pharmaceutical care. Effective communication between pharmacists and practitioners and patients is helpful to build a strong and trusting relationship.

(4) **‘leader’,** where leadership involves the ability to make decisions, manage and communicate effectively, whilst showing compassion and empathy. Effective pharmacy leaders are experts in demonstrating and developing high-performance pharmacy practices characterised by high quality patient care, improved medication safety and maximum productivity.

(5) **‘manager’,** where the pharmacist must effectively manage manpower, physical and financial resources and information, and must be comfortable being managed by others, whether an employer or the leader of a health care team. The pharmacist must assume greater responsibility for sharing information about medicines, ensure the quality of medicines, maintain clinical competency, and perform inpatient care activities.

(6) **‘life-long-learner’,** where the pharmacist’s career must be supported by continuous learning. Pharmacy education in an institution is not complete and professional experience is needed to pursue a lifelong career as a pharmacist. Pharmacists should regularly update knowledge and skills to update with current trends in drug therapy management.

(7) **‘teacher’,** where the pharmacist is responsible for assisting with education and training of future generations of pharmacists and the general public. Participating in teaching offers an opportunity to acquire new knowledge and to improve existing skills (WHO, 1997).

The seven-star pharmacist concept is still applicable and these attributes are considered fundamental for the community pharmacist to be an effective healthcare team member to provide patient-centred pharmacy services (Thamby et al, 2014; Sam et al, 2015).

1.4 Quality aspects in pharmacy practice

Standards are required to ensure optimal and consistent provision of patient-centred community pharmacist interventions, targeted towards quality in patient care. Quality is accomplished when patient care is integrated within current regulations, when services provided, current professional knowledge and outcomes are in harmonisation, and when a cost-effective outcome is achieved (Montgomery et al, 2010; Scicluna et al, 2012; Bugnon et al, 2012; Wirth et al, 2013).

Quality assurance should underlie all professional pharmacy services to ensure standardised provision of services (Azzopardi, 2000; Scicluna et al, 2012; Wirth et al, 2013). The WHO recommends that health systems should strive to make advancements in six areas of quality, which require health care provided to be '**effective'**, by being evidence-based and resulting in improved health outcomes for the community and for individuals; '**efficient'**, utilising resources and avoiding waste; '**accessible',** when necessary in a setting where skills and resources are available as required and geographically-reasonable; '**acceptable and patient-centred'**, on the basis of the individual service users' preferences and cultures of the community; '**equitable'**, provided to all patients in the same manner, irrespective of gender, race, ethnicity, geographical location, or socio-economic status; and '**safe'**, with minimum risks and

harm to service users.[5]

The quality of the services offered at a community level is central for optimal patient care (Azzopardi, 2000; AlGhurair et al, 2012). In a market-oriented and economics-driven society, community pharmacists are faced with the daily struggle of what should be done with each individual patient that will make the experience at a community pharmacy unique (Azzopardi, 2000; Moullin et al, 2013; Moullin et al, 2016). Quality in health care encompasses licensing and certification, compliance to legislation and regulations, performing to meet established standards, and efficiency (Philipsen, 2003; Philipsen, 2014). Quality standards for patient-centred pharmacy services have been developed and quality of pharmacy services has been measured (Azzopardi, 2000). [6]

1.4.1 Good Pharmacy Practice

FIP has been very active in developing the concept of quality systems and quality standards for community pharmacy for many years. FIP was first to develop standards for pharmacy services in 1992, titled 'Good Pharmacy Practice in Community and Hospital Settings'.[6] The standards were developed to be used as a reference by national pharmaceutical organisations, governments and international pharmaceutical organisations to set up nationally-accepted Good Pharmacy Practice (GPP) standards. The GPP guidelines were revised and approved in 1997 by a 'WHO Expert Committee

[5] World Health Organisation. Quality of care: A process for making strategic choices in health systems [Online]. Geneva: World Health Organisation; 2006 [cited 2018 May 30]. Available from: URL: www.who.int/management/quality/assurance/QualityCare_B.Def.pdf?ua=1

[6] World Health Organisation. Good Pharmacy Practice (GPP) in community and hospital pharmacy setting [Online]. Geneva: World Health Organisation; 1996 [cited 2018 May 30]. Available from: URL: http://www.paho.org/bra/index.php?option=com_docman&view=download&alias=805-good-pharmacy-practice-gpp-in-community-hospital-settings-5&category_slug=vigilancia-sanitaria-959&Itemid=965

on Specification for Pharmaceutical Preparations'. FIP endorsed the recommendations made by this committee and published the FIP/WHO joint document on GPP in 1999 in the WHO Technical report series 885 as Annex 7.[7] In 2007, an FIP working group was set up to identify key issues to be considered in the revision of the guidelines to reflect contemporary standards of practice and thinking, and an expert consultation was held in Basel, Switzerland in 2008 during the 68th World Congress of FIP. In 2011, FIP and WHO adopted an updated version of the GPP guidelines titled, 'Joint FIP/WHO Guidelines on Good Pharmacy Practice: Standards for Quality of Pharmacy Services'.[8]

In the 2011 guidelines, GPP is defined as "the practice of pharmacy that responds to the needs of the people who use the pharmacists' services to provide optimal, evidence-based care".[9] Throughout the years, the term pharmaceutical care has established itself as a philosophy of practice with the patient as the primary beneficiary of the pharmacist's interventions. Although the main perceptions of GPP and pharmaceutical care are largely interchangeable, pharmaceutical care is implemented through the concept of GPP.[9]

[7] World Health Organisation. WHO expert committee on specifications for pharmaceutical preparations [Online]. Geneva: World Health Organisation; 1999 [cited 2018 May 30]. p. 93-101. Available from: URL: http://apps.who.int/medicinedocs/pdf/h1792e/h1792e.pdf

[8] International Pharmaceutical Federation. Good Pharmacy Practice: Joint FIP/WHO guidelines on GPP: Standards for quality of pharmacy services [Online]. The Hague: International Pharmaceutical Federation [cited 2018 May 30]. Available from: URL: https://www.fip.org/www/uploads/database_file.php?id=331&table_id=

[9] World Health Organisation. WHO expert committee on specifications for pharmaceutical preparations [Online]. Geneva: World Health Organisation; 2011 [cited 2018 May 30]. p. 310-324. Available from: URL: http://apps.who.int/iris/bitstream/handle/10665/44079/WHO_TRS_961_eng.pdf;jsessionid=4228DDD8EEF0FC68F86CC1F1D3499195?sequence=1

There are four core elements of GPP. The first requires that a pharmacist's primary concern must be the welfare of patients in all settings. Secondly, GPP requires that the core activity of the pharmacist is to help patients make the best use of their medicines. The underlying interventions to implement this requirement include the supply of medicines and other health care products of assured quality, provision of appropriate information and advice to the patient and monitoring the effects of medicine-use. The third requires that an integral part of the pharmacist's contribution is dispensing to ensure the appropriate use of medicines and the promotion of rational and economic prescribing, while the fourth element requires that the pharmacy service is relevant to the patient, clearly defined and effectively communicated in a multidisciplinary collaboration amongst healthcare professionals to all those involved, for successful improvement in patient safety.[6,7,8,9]

[6] World Health Organisation. Good Pharmacy Practice (GPP) in community and hospital pharmacy setting [Online]. Geneva: World Health Organisation; 1996 [cited 2018 May 30]. Available from: URL: http://www.paho.org/bra/index.php?option=com_docman&view=download&alias=805-good-pharmacy-practice-gpp-in-community-hospital-settings-5&category_slug=vigilancia-sanitaria-959&Itemid=965

[7] World Health Organisation. WHO expert committee on specifications for pharmaceutical preparations [Online]. Geneva: World Health Organisation; 1999 [cited 2018 May 30]. p. 93-101. Available from: URL: http://apps.who.int/medicinedocs/pdf/h1792e/h1792e.pdf

[8] International Pharmaceutical Federation. Good Pharmacy Practice: Joint FIP/WHO guidelines on GPP: Standards for quality of pharmacy services [Online]. The Hague: International Pharmaceutical Federation [cited 2018 May 30]. Available from: URL: https://www.fip.org/www/uploads/database_file.php?id=331&table_id=

[9] World Health Organisation. WHO expert committee on specifications for pharmaceutical preparations [Online]. Geneva: World Health Organisation; 2011 [cited 2018 May 30]. p. 310-324. Available from: URL: http://apps.who.int/iris/bitstream/handle/10665/44079/WHO_TRS_961_eng.pdf;jsessionid=4228DDD8EEF0FC68F86CC1F1D3499195?sequence=1

1.4.2 Validation of community pharmacy services

Azzopardi (2000) had the vision to quantitatively measure the quality of professional services provided by community pharmacists and developed a validation process that can be considered in terms of measuring the output of community pharmacy. Azzopardi established the concept of validation in community pharmacy in view to enhance pharmacy practice in the challenging area of community pharmacy. Azzopardi developed an internal validation process which monitors the standards of professional services from within the profession itself, and an external validation process to confirm the need for community pharmacist interventions towards patient care from outside the profession, by studying the perception of consumers and other health care professionals.

Azzopardi presented the validation process and validation tools in a philosophical perspective as the 'cure' to the malaises that surround the community pharmacy profession, where the malaises were identified as the strengths and weaknesses of community pharmacy practice. The strengths of community pharmacy were identified as community pharmacy being a large workforce and community pharmacists as easily accessible health care professionals, whilst the weaknesses were the apparent loss of the traditional role of the community pharmacist, de-professionalisation of community pharmacy and that the community pharmacist is not demonstrating a valid enough contribution towards patient care (Azzopardi, 2000). The validation in community pharmacy concept is dynamic and was updated by Buttigieg (2006), Scicluna et al (2012) and Flynn (2017).

1.5 The gap between the community pharmacy profession and the regulatory body

Regulation of the community pharmacy profession is important to safeguard the patient, however a problem with respect to regulation of the pharmacy profession is that regulation has not yet adapted to community pharmacist services in 'modern' health care. Since provision of pharmaceutical care is fundamental in 'modern' pharmacy practice, regulatory bodies should adapt to incorporate pharmaceutical care aspects into regulation (Cousins et al, 2012).

Significant regulatory structures have been implemented to ensure the quality and safety of medicines in Europe and worldwide (Cousins et al, 2012), however there is increasing evidence that the inappropriate use of medicines may result in suboptimal medication outcomes and decreased effectiveness in healthcare systems (Holloway, 2011; Ofori-Asenso et al, 2016). Regulatory authorities should implement pharmaceutical care in their regulatory frameworks to assure distribution of medicines of high quality and safety and to ensure provision of optimal care to patients (Cousins et al, 2012).

A regulatory authority, supported by a complex legal framework, is a government authority, responsible to ensure that all legal requirements are met. A policing approach by the regulator promotes negativity, does not support communication and cooperation and is a cause of non-compliance to regulation (Shapiro et al, 1997; Wiederholt et al, 2002). Communication and cooperation is supported by education and theoreticians and practitioners of adult education acknowledge that educational approaches improve human performance (Shapiro et al, 1997; Wiederholt et al, 2002). In the context of this research,

improving ‘human’ performance relates to improving ‘pharmacist’ performance towards regulation and in the provision of pharmaceutical care.

1.6 Philosophical theories and concepts related to educational approaches

Analysing philosophical theories and concepts is essential to understand the difference between policing and educational approaches and the outcomes associated with each approach. The community pharmacist is an ‘adult’, hence identifying the best learning methods and techniques to engage ‘adult learners’ is required. Berwick (1989) suggested two theories of quality that describe the climate in which care is delivered, namely ‘The Theory of the Bad Apple’ and ‘The Theory of Continuous Improvement’.

1.6.1 Berwick’s Theories in relation to quality of care

In the New England Journal of Medicine in 1989 Berwick explains the ‘The Theory of the Bad Apple’ and ‘The Theory of Continuous Improvement’ using an example of two assembly lines being monitored by two foremen. Berwick described the first foreman as watching carefully over the workers and looking to find unprepared and unwilling-to-work workers to punish them and instil negativity, whilst the second foreman watches the workers but instead instils positivity by praising their work. The first foreman represents ‘The Theory of the Bad Apple’, while the second foreman represents ‘The Theory of Continuous Improvement’. The task of the latter foreman is to identify opportunities for improvement amongst the workers, to find skills that could be shared and lessons to be learned, and to provide a means to improve the work for all workers and not the exceptional few at either end of the spectrum of competence (Berwick, 1989). These

theories can be applied to the regulation of community pharmacy, where there are two approaches to improving quality; a policing approach and an educational approach.

'The Theory of the Bad Apple' suggests that quality is best achieved by discovering the 'bad apples' and removing them from the rest; in the case of pharmacy practice regulation, using disincentives to improve quality, such as publication of reprimands, fines and forfeitures levied to pharmacists (Berwick, 1989; Wiederholt et al, 2002). A policing approach is represented by 'The Theory of the Bad Apple', where the regulator looks for 'bad' or 'suboptimal' pharmacy practice (Wiederholt et al, 2002). Berwick proposed that deficiencies in quality, including non-compliance to pharmacy regulations, are not attributed to lack of will, skill or effort of a pharmacist, but rather to poor job design, leadership failure or unclear purpose by the regulator. Quality in pharmaceutical care provision can be improved when the pharmacist is viewed as capable and not accused of indolence, as suggested by a policing approach (Wiederholt et al, 2002). For many pharmacists, a policing approach may instigate fear, hence inhibiting improvement in the quality of patient care provided. Such a policing approach is likely to lead to disaffection towards the regulatory authority, distortion of information such as falsified records, and a decreased opportunity to learn (Berwick, 1989; Shapiro et al, 1997; Wiederholt et al, 2002).

The 'Theory of Continuous Improvement' suggests that real improvement in quality depends on understanding and revising processes according to data about the processes themselves (Berwick, 1989). An educational approach to enforcement and regulation seeks continuous improvement in pharmacy practice (Wiederholt et al, 2002). The

‘modern’ quality improvement regulator should focus more on learning and educational cooperation with the pharmacist rather than on improvement through only disciplinary measures (Shapiro et al, 1997; Wiederholt et al, 2002).

1.6.2 The concept of andragogy

From Berwick’s theories it can be established that an educational approach is more favourable than an enforcement approach and seeks cooperation with the pharmacist towards positive patient care outcomes. The community pharmacist is an ‘adult’ and different teaching methods should be explored to engage the pharmacist in the learning process. Malcolm Knowles, an adult educator, developed the concept of ‘Andragogy’ and is associated with popularising and operationalising this concept defined as ‘the art and science of helping the adult learn’ (Knowles, 1985; Holyoke et al, 2009; Knowles et al, 2015). In contrast, pedagogy is the traditional method of instruction, where the learner is dependent on the teacher, and the teacher determines what and when information will be learned and how it will be learned (Flores et al, 2016). In andragogy, adult learners are viewed as being capable since they have had more life experiences (Taylor, 1999; Hagen et al, 2016). Unlike pedagogy, andragogy puts the focus on the learner, that is, on the adult and not on the teacher (Flores et al, 2016). In the context of this research, the adult learner is the community pharmacist.

In the 1980s, Knowles made four critical assumptions about the characteristics of adult learners that differ from the assumptions of pedagogy. In 1984, he added the fifth assumption and these were later expanded to the six assumptions of the andragogical

model which form part of a learning theory system (Knowles, 1985; Holyoke et al, 2009; Knowles et al, 2015; Flores et al, 2016).

The first assumption of andragogy is that adults are '**self-directed learners'**. As a person matures, the 'self'-concept transforms from being a dependent learner to becoming increasingly self-directing. Adult learners increasingly take the initiative to diagnose their own learning needs, hence the role of the teacher is to engage the adult in a process of mutual enquiry rather than to transmit knowledge to them. The second assumption is that adults are **'experienced'**. Experience develops the identity and self-image of an individual. The learning process should build upon the experiences and knowledge of the adult and should be considered as a resource to filling gaps in knowledge. The third assumption is the adult's **'readiness-to-learn'**. An adult is more focused on learning opportunities and outcomes that will address areas of development to improve performance. A change is likely to trigger the adult to learn, hence the learning process should be focused on assessing gaps in the current versus a proposed situation, engaging the adult to perform more effectively to reach what is proposed.

The fourth assumption of the andragogical model is that adults are **'oriented towards learning'**. Adults regard learning as a process to improve their ability and competence to solve current situations, hence the learning process should incorporate real-life situations. The fifth assumption is that adults **'need to know the reason'** for learning something. This assumption is a continuation of the fourth, where the adult is oriented towards learning when the adult knows the reason for learning. The learning process should be problem-oriented and should engage the adult to learn. The last assumption is that the

adult should be **'motivated to learn'**. Knowles believed that adults are best motivated to learn when they are recognised and appreciated for their contribution. Hence acknowledging contributions and success should form the basis of a learning model to motivate the adult learner (Knowles, 1985; Holyoke et al, 2009; Knowles et al, 2015; Flores et al, 2016).

Other factors may affect adult learners to behave closely to the assumptions of andragogy, including individual and situational differences, goals and purposes for learning. These andragogy assumptions work best in practice when they are adapted to fit the uniqueness of the learning situation and the individual learner and can be applied in all adult learning situations, provided they are considered in relation to other factors that may be present in a situation (Knowles et al, 2015; Flores et al, 2016).

Following analysis of the value of an educational approach and identification of the learning theory system for the adult, techniques that can lead adult learners to engage in the learning process are identified. The great teachers of ancient times - Confucius and Lao Tso in China, the Hebrew prophets and Jesus in biblical times, Aristotle, Socrates and Plato in ancient Greece, and Cicero, Evelid and Quintilian in ancient Rome - recognised learning to be a process of enquiry and a process of mental questioning and investigation, rather than the passive acquisition of transmitted information (Crowley et al, 1999; Knowles et al, 2015). Since their experiences were with adults, they developed different learning concepts than those of formal education of children. The techniques they developed were aimed at engaging learners in enquiry (Knowles et al, 2015).

The ancient Chinese and Hebrews conceived what is referred to as 'the case method' (Knowles et al, 2015). This approach involves the description of a situation by the leader or a member of the group, often in the form of a parable, and together its characteristics are explored and possible solutions are identified (Crowley et al, 1999; Knowles et al, 2015). The Greeks developed the 'Socratic dialogue', which involves a question or dilemma posed by the leader or a member of the group, with the members of the group pooling their experience and thinking to find a possible solution. The Romans were more confrontational, where challenges were used to force group members to state a position and then defend them (Crowley et al, 1999; Knowles et al, 2015).

1.7 The evolution from paternalistic medicine to patient empowerment: From compliance and adherence to concordance

Berwick's 'Theory of Continuous Improvement' suggests an educational approach, whereby the regulator should focus on learning and collaborating with the pharmacist to reach an agreement through cooperation and education (Berwick, 1989; Wiederholt et al, 2002). Terminologies used in medicine-taking, moving from compliance and adherence to concordance, are analysed to better understand the concept of an educational approach to regulation versus a policing approach.

Medicine-taking has been described using three seemingly related terms namely; compliance, adherence and concordance (Chakrabarti, 2014). However, these terms are different and have evolved to capture emerging ideas, practices and discoveries in medicine (Bell et al, 2007).

Compliance is defined as “the extent to which the patient behaviour matches the prescriber’s recommendations” (Horne et al, 2005; Chakrabarti, 2014). Compliance suggests a one-sided interaction, where the practitioner decides on a suitable treatment to which the patient must comply (Chakrabarti, 2014). Compliance may imply a submissive attitude and lack of patient involvement in a paternalistic setting (Horne et al, 2005). This can be likened to the policing approach to regulation, whereby the pharmacist must comply to regulation. In medicine-taking, use of the term ‘compliance’ declined and was replaced by the term ‘adherence’ (Horne et al, 2005).

Adherence is defined as “the extent to which a person’s behaviour, corresponds with agreed recommendations from a health care professional” (Horne et al, 2005; Bissonette, 2008). Adherence has been adopted as an alternative term to compliance in an attempt to introduce the emphasis that a patient is empowered to decide whether or not to adhere to a prescriber’s recommendations by emphasising the need for an agreement. However, the evolution from compliance to adherence in medicine did not address a patient’s decision, hence to overcome this issue, the term ‘concordance’ is being used with respect to medicine-taking.

The term ‘concordance’ was first used in the context of medicine in 1997, when the Royal Pharmaceutical Society of Great Britain published a document titled ‘From Compliance to Concordance: Towards Shared Goals in Medicine Taking’ (Marinker et al, 1997; Foster et al, 1998; Britten, 2007). The report was written by a working party with the aim to review the causes and consequences of non-compliance and non-adherence and propose recommendations (Marinker et al, 1997; Foster et al, 1998). Concordance was

first applied in the consultation process in which the prescriber and the patient engage in discussion, whereby the views of both parties, especially the patient's views, are considered (Sanz, 2003; Weiss et al, 2009; Snowden et al, 2013). Concordance has expanded to include patient support in medicine-taking, effective communication with the patient, and offering support to the patient throughout the treatment process (Chakrabarti, 2014).

The principal element of concordance is the establishment of a positive collaboration between the prescriber and the patient (Watson, 2009; Snowden et al, 2013). An educational approach suggests concordance, whereby an agreement is reached through cooperation and positive collaboration. Concordance is not synonymous with compliance nor adherence (Bell et al, 2007; De Las Cuevas, 2011). The evolution from compliance and adherence to concordance is a patient-centred concept as this represents progress in understanding the patient's perception of medicine-taking (Bell et al, 2007; De Las Cuevas, 2011). Concordance in clinical practice can be a way by which non-adherence can be better understood and addressed through reaching an agreement (Bell et al, 2007). In medicine-taking, compliance and adherence can be estimated using pharmacy dispensing data, electronic pill counters, prescription claim records and directly by measurement of drug serum levels. There are no acceptable, valid or reliable tools to measure concordance in the context of medicine-taking (Bell et al, 2007).

1.8 The audit process

Community pharmacy activities are regulated through regulatory audits. An audit is an on-site verification activity, such as an inspection or examination, of a process or quality system to ensure compliance to stipulated requirements (Russell, 2013). As defined by International Organisation for Standardisation (ISO) 9000:2015, an audit is a "systematic, independent and documented process for obtaining audit evidence (records, statements of facts or other information) and evaluating it objectively to determine the extent to which the audit criteria are fulfilled".[10] An audit is systematic since it is methodological, performed according to a fixed plan, and independent, since the auditor must be independent, avoiding conflicts of interest and ensuring high integrity audits (Russell, 2013). The type of audit carried out depends on the purpose of the audit. There are 'compliance/conformance' audits, 'performance' audits and 'follow-up' audits. 'Compliance/conformance' audits ensure that the auditee management system complies with the requirements of a pertinent standard or regulation and may result in certification. For example, medical devices must comply to the Conformité Europeënne mark requirements for certification (Russell, 2013). In community pharmacy regulatory audits (CPRAs), a pharmacy license certificate is issued if the pharmacy complies/conforms to regulation.

'Performance' audits go beyond the traditional 'compliance/conformance' audits and are designed to promote improvement. A key difference between 'compliance/conformance' audits and 'performance' audits is the collection of evidence related to the performance

[10] International Organisation for Standardisation. Quality management systems-Fundamentals and vocabulary [Online]. International Organisation for Standardisation; 2015 [cited 2018 May 30]. Available from: URL: https://www.iso.org/obp/ui/#iso:std:iso:9000:en

of the auditee versus evidence collection to ensure compliance to a standard, procedure or regulation. Audits that assess only compliance and conformance do not provide results on the quality of performance. 'Performance' audits may result in findings that require corrective and/or preventive actions (CAPAs). Since most CAPAs cannot be implemented during an ongoing performance audit, a follow-up audit may be required to verify that CAPAs were executed (Russell, 2013).

There are four phases of an audit, namely preparation, performance, reporting and follow-up/closure. Audit preparation involves preparing for the audit in advance to ensure that the audit undertaken complies with the identified objective. The preparation phase of an audit begins with the decision to conduct an audit until commencement of the audit. The performance phase of an audit is also referred to as 'fieldwork' and is the data-gathering phase of an audit covering the time period between arrival at the audit location to the concluding meeting. The audit report must communicate the findings of the audit and an audit process ends when the report is issued (Russell, 2013). ISO 9000:2015 specifies that an audit is complete when all the planned activities have been carried out, agreed upon with the auditee, or by verification of follow-up actions by a subsequent compliance/conformance or performance audit.[10]

[10] International Organisation for Standardisation. Quality management systems-Fundamentals and vocabulary [Online]. International Organisation for Standardisation; 2015 [cited 2018 May 30]. Available from: URL: https://www.iso.org/obp/ui/#iso:std:iso:9000:en

1.8.1 Community pharmacy regulatory audits in Malta

The Malta Medicines Authority (MMA), the regulatory body in Malta, performs CPRAs. Prior to this research, community pharmacies in Malta were assessed using a compliance/conformance audit approach, where an audit was carried out to verify that licence conditions stated in the Medicines Act[11] and Subsidiary Legislation 458.16[12], 458.28[13], 458.49[14], 458.53[15] and 458.58[16] are met. CPRAs ensured that patients were supplied with medicines of the right quality, safety and efficacy, such as through maintenance of the correct storage conditions[17] and performance towards professional pharmacy services were not being assessed in CPRAs prior to this research. The CPRA is carried out by two pharmacists employed at the MMA, taking the roles of lead auditor and accompanying auditor. Two auditors carry out the CPRA to countercheck each other. Following the audit and after analysing the findings, the auditors decide on a course of action. The decision may involve five options, namely the issue of a warning letter based on pre-set standard criteria, requesting a meeting at the MMA, maintaining contact with

[11] Ministry for Justice, Culture and Local Government. Chapter 458 Medicines Act [Online]. Malta: The Ministry; 2003 [cited 2018 May 30]. Available from: URL: http://www.justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=8924&l=1

[12] Ministry for Justice, Culture and Local Government. Subsidiary Legislation 458.16 Pharmacy License Regulations [Online]. Malta: The Ministry; 2007 [cited 2018 May 30]. Available from: URL: http://www.justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=11256&l=1

[13] Ministry for Justice, Culture and Local Government. Subsidiary Legislation 458.28 Pharmacies Opening Hours Rules [Online]. Malta: The Ministry; 2010 [cited 2018 May 30]. Available from: URL: http://www.justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=11268&l=1

[14] Ministry for Justice, Culture and Local Government. Subsidiary Legislation 458.49 Prescription and Dispensing Requirements Rules [Online]. Malta: The Ministry; 2006 [cited 2018 May 30]. Available from: URL: http://www.justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=11287&l=1

[15] Ministry for Justice, Culture and Local Government. Subsidiary Legislation 458.53 Pharmacy Licenses (Fees) Regulations [Online]. Malta: The Ministry; 2008 [cited 2018 May 30]. Available from: URL: http://www.justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=11291&l=1

[16] Ministry for Justice, Culture and Local Government. Subsidiary Legislation 458.58 Pharmacy License (Transfer) Regulations [Online]. Malta: The Ministry; 2014 [cited 2018 May 30]. Available from: URL: http://www.justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=12268&l=1

[17] Malta Medicines Authority. Pharmacies [Online]. Malta: Malta Medicines Authority; 2018 [cited 2018 May 30]. Available from: URL: http://medicinesauthority.gov.mt/Pharmacies

the pharmacist via electronic mail, carrying out a follow-up audit, or no follow-up may be required. More than one decision can be taken for the same audit. The pharmacist will be informed regarding the course of action at the time of the CPRA.

Five types of CPRAs are performed which include[17]:

- **New application audits -** carried out when a new application to open a pharmacy is received by the MMA and an audit follows to issue a 'List of Works' that need to be carried out to ensure that the premises are in accordance with the required standards. These audits are notified in advance.
- **Variation audits -** carried out following receipt of a variation of an existing pharmacy license, such as a change in location of the pharmacy. Not all variations require an audit since some variations are only administrative, such as a change in the managing pharmacist or a change in the license holder. These audits are notified in advance.
- **Renewal audits -** carried out every two years according to a pre-set audit plan to be able to renew the pharmacy license issued by the MMA. These audits are not notified in advance. During this type of audit, the routine CPRA takes place.
- **Spot-check audits -** carried out following receipt of a complaint from a patient, pharmacist or stakeholder. These audits are not notified in advance.
- **Follow-up audits**
    a) **Type a -** follow-up after the submission of a new application, usually carried out following the issue of a 'List of works' to check for compliance. These audits are notified in advance.

[17] Malta Medicines Authority. Pharmacies [Online]. Malta: Malta Medicines Authority; 2018 [cited 2018 May 30]. Available from: URL: http://medicinesauthority.gov.mt/Pharmacies

b) **Type b -** follow-up after a CPRA carried out to confirm that CAPAs implemented following findings during a renewal or spot-check CPRA, are addressed. These audits are not notified in advance.

A pharmacy audit tool is always used for renewal CPRAs and may be used for spot-check and follow-up audits type b. The audit tool used by the MMA during CPRAs was last updated in 2012. The audit tool consisted of 15 points with space for remarks. The first 3 points covered administrative data, namely name and address of dispensary, licence holder and managing pharmacist details. Point 4 to 6 assessed whether the pharmacist is present for the CPRA and the appearance of the pharmacist, including wearing a white coat and identification badge. Point 7 relates to the condition of the premises and checked whether records for cleaning of premises, pest control and temperature monitoring are being kept. Point 8 checked whether temperature monitoring devices are calibrated, and point 9 checked whether the refrigerator is being used solely to store medicines. Other registers or records were checked in point 10, including the daily medicines register, dangerous drug purchases and sales registers and locum pharmacist register. Point 11 checked where the key for the dangerous drugs cupboard is kept and point 12 checked the condition of utensils used to prepare extemporaneous medicines. Point 13 checked the storage condition of medicines and point 14 checked dangerous drugs prescriptions. The last point verified whether medicines are being purchased from authorised wholesale dealers. The space for remarks was allocated at the end of the tool. The tool was signed by the auditors and practicing pharmacist with the date noted.

1.9 Rationale for the research

There is a gap between the community pharmacy profession and the regulatory body and this gap can be addressed by evolving the approach of CPRAs to focus more on pharmaceutical care provision. This evolvement should reflect the incorporation of a patient-centred, educational approach during CPRAs to reach cooperation and concordance between the pharmacist and the regulator in the interest of patient safety.

The gap between the evolvement of the pharmacy profession and its regulation is addressed in this research by employing an educational approach in CPRAs as suggested by Berwick's 'Theory of Continuous Improvement', adopting the assumptions of the concept of andragogy to reach concordance to regulation, and to enhance provision of pharmaceutical care through techniques that engage pharmacists to learn. The audit purpose in this research goes beyond compliance and conformance to regulation and incorporates the assessment of performance towards patient-centred care in community pharmacy and to reach concordance between the pharmacist and the auditor on CAPAs to improve patient safety.

1.10 Research Questions

The research questions addressed were:

- Can concordance in CPRAs be reached through employing an educational approach rather than forceful enforcement?
- Can concordance in CPRAs lead to optimised patient-centred practice?

1.11 Aim and Objectives

The aim of this research was to develop and implement patient-centred regulatory audits in community pharmacy.

The objectives were to:

(1) Retrospectively analyse CPRA reports

(2) Update and validate the audit tool used in CPRAs

(3) Implement the updated tool in CPRAs and identify beneficial patient-related improvements in community pharmacy practice

(4) Evaluate case studies to recommend improvements to patient safety in community pharmacy practice.

Chapter Two

Methodology

2.1 Overview

The methodology consisted of literature and legislation review, retrospective analysis of community pharmacy regulatory audit (CPRA) reports and interviews with community pharmacists which formed the basis for development of an updated CPRA tool, validation of the CPRA tool, implementation of the tool during CPRAs, identification of deficiencies related to patient safety, and evaluation of case studies on the identified deficiencies (Figure 2.1).

2.2 Research design

A quantitative research approach was used in the retrospective analysis of CPRA reports and in the analysis of findings from CPRA implementation. A qualitative approach was adopted by conducting one-to-one interviews with community pharmacists to develop the CPRA tool and by carrying out direct observation during the CPRAs to identify deficiencies and evaluate case studies to recommend improvements to patient safety.

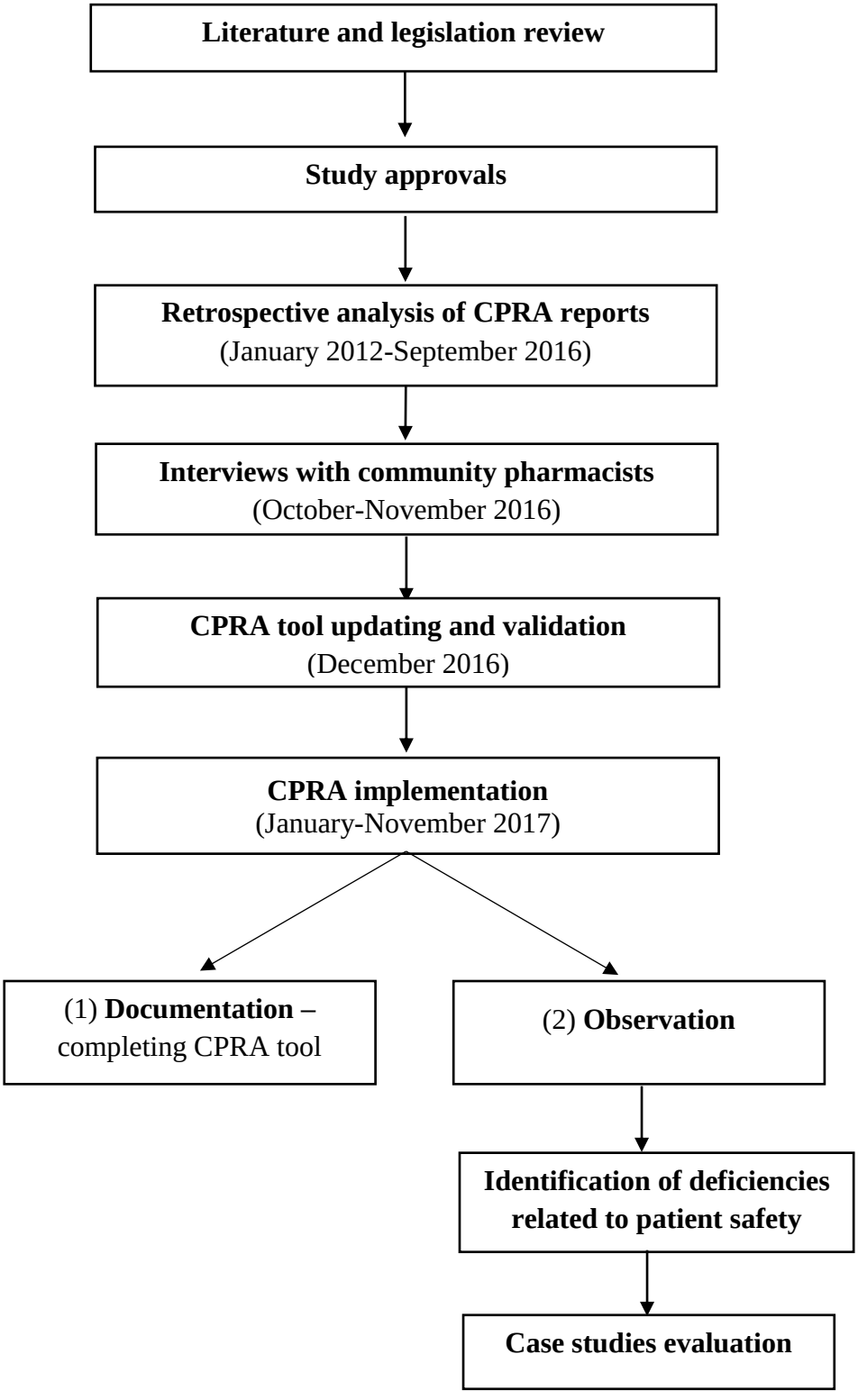


Figure 2.1: Flowchart of research methodology

2.3 Literature and legislation review

Legal sources consulted were the Medicines Act, enshrined in Chapter 458 of the Laws of Malta[11], and Subsidiary Legislation 101.02[18], 458.16[12], 458.28[13], 458.49[14], 458.53[15] and 458.58[16]. Standard Operating Procedures (SOPs) governing CPRAs at the Malta Medicines Authority (MMA) were reviewed. Articles relevant to the research topic were retrieved from PubMed® database, Google Scholar literature library and HyDi Hybrid Discovery search gateway of the University of Malta and reviewed. Key words and phrases for the literature search included: Audit; community pharmacist interventions; community pharmacy; concordance; educational approaches; evolution of community pharmacy; good pharmacy practice; patient-oriented practice; pharmaceutical care; philosophical theories of education; policing approach; product-oriented approach; quality in community pharmacy; regulatory audits; regulatory reform. Relevant books, reports and dissertations were reviewed.

[11] Ministry for Justice, Culture and Local Government. Chapter 458 Medicines Act [Online]. Malta: The Ministry; 2003 [cited 2018 May 30]. Available from: URL: http://www.justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=8924&l=1

[18] Ministry for Justice, Culture and Local Government. Subsidiary Legislation 101.02 Internal Control of Dangerous Drugs Rules [Online]. Malta: The Ministry; 1939 [cited 2018 May 30]. Available from: URL: http://www.justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=9261&l=1

[12] Ministry for Justice, Culture and Local Government. Subsidiary Legislation 458.16 Pharmacy License Regulations [Online]. Malta: The Ministry; 2007 [cited 2018 May 30]. Available from: URL: http://www.justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=11256&l=1

[13] Ministry for Justice, Culture and Local Government. Subsidiary Legislation 458.28 Pharmacies Opening Hours Rules [Online]. Malta: The Ministry; 2010 [cited 2018 May 30]. Available from: URL: http://www.justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=11268&l=1

[14] Ministry for Justice, Culture and Local Government. Subsidiary Legislation 458.49 Prescription and Dispensing Requirements Rules [Online]. Malta: The Ministry; 2006 [cited 2018 May 30]. Available from: URL: http://www.justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=11287&l=1

[15] Ministry for Justice, Culture and Local Government. Subsidiary Legislation 458.53 Pharmacy Licenses (Fees) Regulations [Online]. Malta: The Ministry; 2008 [cited 2018 May 30]. Available from: URL: http://www.justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=11291&l=1

[16] Ministry for Justice, Culture and Local Government. Subsidiary Legislation 458.58 Pharmacy License (Transfer) Regulations [Online]. Malta: The Ministry; 2014 [cited 2018 May 30]. Available from: URL: http://www.justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=12268&l=1

2.4 Setting and approvals

The research was carried out with the MMA, whose objective is to enhance public health through the regulation of medicines and pharmaceutical activities.[19] There are four Directorates within the MMA, namely the 'Licensing Directorate', 'Post-Licensing Directorate', 'Inspectorate and Enforcement Directorate', and 'Strategy, Operations and Regulatory Affairs Directorate'. This research was undertaken within the Inspectorate and Enforcement Directorate (IED), which is responsible for the auditing of wholesalers, manufacturers/importers, retail and non-retail pharmacies, issue of licenses, renewals and variations, and enforcement in line with the Medicines Act 2003 and its Subsidiary Legislation. In Malta, there are 229 retail community pharmacies, 5 national hospital pharmacies, 4 private in-patient pharmacies, and the non-governmental organisation Sedqa Pharmacy.[17] This research was carried out in retail community pharmacies. Approval from the Chairman of the MMA and the Director of the IED to carry out the research was granted. No ethical approval was required.

[19]Malta Medicines Authority. Mission and Objectives [Online]. Malta: Malta Medicines Authority; 2018 [cited 2018 May 30]. Available from: URL: http://medicinesauthority.gov.mt/missionobjectives?l=1

[17] Malta Medicines Authority. Pharmacies [Online]. Malta: Malta Medicines Authority; 2018 [cited 2018 May 30]. Available from: URL: http://medicinesauthority.gov.mt/Pharmacies

2.5 Retrospective analysis of CPRA reports

A retrospective analysis of retail CPRA reports was carried out to extract features in the reports that could lead to the lack of identification of patient-related deficiencies. A file for each community pharmacy in Malta and Gozo is kept at the MMA. The file contains documents from the time the application to open the community pharmacy was submitted, including variation applications, CPRA reports, follow-up CPRA reports, electronic mail communication and any legal notifications. The file for each retail community pharmacy was obtained and CPRA reports were reviewed. Criteria for the extraction of data were set to ensure conformance of data obtained from each CPRA report, namely findings, corrective actions, integrity of the report and if they were complete, and follow-up CPRA reports, if any. CPRA reports for the period January 2012 to September 2016 were analysed. January 2012 was chosen on the basis of the last update to the tool that was being used by the MMA for CPRAs.

2.6 Interviews with community pharmacists

Informal one-to-one interviews with twelve community pharmacists were performed during CPRAs in October and November 2016. Two pharmacists from each of the six statistical districts in Malta (Southern Harbour, Northern Harbour, South Eastern, Western, Northern, Gozo and Comino[20]) were interviewed. The pharmacists could not have been selected according to age, gender and experience, since the CPRAs are unannounced and the auditor is unaware of the pharmacist who will be encountered. The

[20] National Statistics Office. Regional Statistics Malta: 2017 edition [Online]. Malta: National Statistics Office; 2017 [cited 2018 May 30]. Available from: URL: https://nso.gov.mt/en/publicatons/Publications_by_Unit/Documents/02_Regional_Statistics_(Gozo_Office)/Regional%20Statistics%20MALTA%202017%20Edition.pdf

interviews were performed with the pharmacist present at the time of the CPRA to identify patient-related improvements to the CPRA. Recommendations from the pharmacists were used to update the CPRA tool and to develop criteria for the observation during CPRA implementation. The interviews were performed in the context of an ongoing CPRA since opinions and recommendations of the pharmacists would reflect the experience of an actual CPRA, increasing accuracy and reliability of data collection.

The researcher asked two open-ended questions to stimulate a discussion with the pharmacist. Each pharmacist was asked: 'What are the limitations of the present CPRA? and 'How can the present CPRA be improved to ensure patient safety and improve professional community pharmacy activities?'

2.7 Updating and validation of the CPRA tool

Findings from the retrospective analysis, recommendations from the interviews with the community pharmacists and information from the literature and legislation review were used to update the CPRA tool. Updates to the CPRA tool and the rationale for the updates are described in Appendix 1. The updated audit tool consists of seven sections (A – G) (Table 2.1).

Table 2.1: CPRA tool sections

Section	Title
A	Dispensary details
B	Change in pharmacy license details
C	Name, registration number and contact details of managing pharmacist
D	Name, registration number and contact details of locum pharmacist
E	Signature of managing or locum pharmacist
F	Checklist
G	Auditors signatures and date

Sections A to E are of an administrative nature and section F (Checklist) relates to the legislation/regulation of community pharmacy practice. The checklist is technical, has a legislative/regulatory basis and assesses compliance and conformance to legislation/regulation during the CPRA. The checklist consists of ten subsections in table format, comprising five columns; subsection number, subsection title, yes/no questions and comments. A total of 58 'yes/no' questions were included in the checklist (Table 2.2). The updated CPRA tool consists of 9 A4 pages with Times New Roman font type, 12 point, with 1.5 line spacing for text and 1.15 line spacing for the checklist (Section F).

Table 2.2: Checklist section in the CPRA tool

Subsection number	Subsection title	Number of yes/no questions	Description
1	Standard Operating Procedures	1	Checks for the availability of SOPs at the pharmacy
2	Storage of medicinal products	11	Checks storage of medicines in the pharmacy, refrigerator/s and store/s, calibration of thermometers, servicing of air conditioner/s, temperature records for ambient and refrigerator temperature and expired medicines
3	Locum register and the pharmacist	3	Checks appearance of pharmacist (white coat and identification tag) and locum register
4	Daily medicine dispensing register	4	Checks records in daily medicines register and format, availability of scanned or hard copy prescriptions
5	Dangerous drugs registers	7	Checks dangerous drugs sales and purchases records for private and Pharmacy-Of-Your-Choice medicines and format and expired dangerous drugs
6	Dangerous drugs stock take	1	Confirms whether a dangerous drugs stock take is performed on a yearly basis

Subsection number	Subsection title	Number of yes/no questions	Description
7	Dangerous drugs cupboard	5	Checks whether a lockable dangerous drugs cupboard is available and storage of expired dangerous drugs
8	Extemporaneous preparations	11	Optional section; If carried out, checks for utensils, labels and dedicated area for extemporaneous preparations; if not carried out checks for availability of graduated cylinder and tablet counter
9	Premises	12	Checks general upkeep of the pharmacy, cleaning records and pest control certificate covering all areas
10	Miscellaneous	3	Checks availability of reference books and internet access, sharps bin and designated area for segregation of medicines that are expired or are for disposal

A checklist consisting of 'yes/no' questions was introduced to provide definite responses, where 'yes' implies compliance/conformance and 'no' implies identification of a deficiency. Each question in the checklist was mapped with legislation/regulation and highlighted in red to facilitate the educational approach during the CPRA i.e. to facilitate explanation of the basis for each requirement in the checklist to the pharmacist and is completed by ticking 'yes' or 'no', and where applicable comment/s can be documented.

Validation is important to test whether the developed tool actually measures what it is designed to measure (Azzopardi, 2000; Smith, 2002). Both face and content validity of the CPRA tool were tested. The updated CPRA tool was validated by a panel consisting of ten members, namely the Director of the IED at the MMA, all seven auditors at the MMA and two community pharmacists (one managing pharmacist and one locum pharmacist). The panel members were given one week to complete the validation exercise. The audit tool was validated with respect to layout, comprehensiveness, content and comprehensibility. Feedback was considered to develop the final version of the CPRA tool. The only recommendation by one of the auditors was to check for availability of an 'electronic' balance rather than 'any' balance. The final version of the CPRA tool was included in the quality management system of the MMA as an approved and official document of the MMA (Appendix 2).

2.8 Implementation of the CPRAs

The CPRAs were conducted between January and November 2017, on weekdays, between 9.00 and 12.00 during regular pharmacy opening hours, usually three times/week. The estimated time taken to execute each CPRA was recorded, starting upon entering the pharmacy until exiting the pharmacy.

2.8.1 Selection of retail community pharmacies

The IED of the MMA issues a yearly audit plan with the aim to identify the workload, resources available and capacity of the auditors to fulfil the obligations expected of them. Section 9 of the audit plan governs the assignment of CPRAs and comprises a list of all retail community pharmacies in Malta and Gozo, listed alphabetically according to location. The pharmacies are divided into eight groups; each group is assigned two auditors at the MMA to perform the audits for that particular group of pharmacies. The audit plan was reviewed and all 81 community pharmacies scheduled for a CPRA in 2017 were selected. The audits were executed by the researcher taking the role of lead auditor together with an accompanying auditor. The auditors received training by the Director of the IED.

2.8.2 Inclusion and exclusion criteria of the audits

The audits included in this research were renewal audits, spot-check audits and follow-up audits type b. These audits were selected since they may lead to observation of deficiencies related to patient safety in community pharmacy practice. The audits were followed-up to check for implementation of corrective and preventive actions (CAPAs).

New application audits, variation audits and follow-up audits type a were excluded since these audits are administrative and do not lead to any patient-related observations.

2.8.3 The CPRA process

The CPRA consisted of preparation, on-site fieldwork, issuing the audit report, follow-up communication and closing the audit. Preparation involved identifying the pharmacies to be audited from the audit plan, printing copies of the CPRA tool and reviewing past CPRA reports of the identified pharmacies. On-site fieldwork consisted of two parts namely; (1) documentation and (2) observation, with an educational approach implemented throughout the CPRA.

2.8.3.1 Documentation

Documentation consisted of completing the CPRA tool; completion of administrative data (Section A – D) and the checklist (Section F). Each question in the checklist was marked 'Yes' or 'No' according to the finding during the CPRA. The comments section was filled in according to deficiencies requiring documentation, such as actual temperature readings, dates when registers were last updated and CAPAs that need to be implemented to address deficiencies identified. An educational approach by the auditors was implemented throughout this documentation by explaining to the pharmacist the importance of each activity being audited and, if required, how the activity can be improved. The CPRA tool was completed simultaneously by the lead auditor and the accompanying auditor, providing a copy of the audit tool to be filed at the MMA as an official document and the other for the pharmacist.

2.8.3.2 Observation

Observation by the auditor, incorporated in the CPRA as part of the onsite fieldwork to assess performance towards patient care and safety, was the innovative aspect of this research, as distinct from previous CPRAs. Direct observation is an accurate, reliable and highly selective method of observation. Direct observation relies heavily on the observer, the auditor/researcher in this case, to act as a research instrument, ensuring data collection is more complete (Haw et al, 2007; Stuchberg et al, 2007; Chua et al, 2009; Wirth et al, 2013).

Observation criteria were set according to patient-centred interventions by the community pharmacist identified from the literature review and from the results of the interviews with the community pharmacists. The six observation criteria were:

- Communication skills with patients, staff and other healthcare professionals
- Medication control, including medication errors, dispensing without prescription
- Drug therapy monitoring
- Advice provision
- Pharmacist accessibility to patients
- Equitable treatment, on the basis of race, gender, religion, age and sexual orientation.

During the observation it was ensured that the activities of the pharmacist were not disrupted by the auditors as much as possible, a phenomenon known as the Hawthorne effect (Emmerton et al, 1998). The CPRA was performed with intervals, allowing the pharmacist to attend to patients who visit the pharmacy during the time of the CPRA.

Observation was performed when the pharmacist was attending to patients. The auditor adapted to the environment of each pharmacy and found a suitable location where all activities being undertaken by the pharmacist were visible and at the same time attempted to be as inconspicuous as possible. The auditor did not stand next to entrances so as not to obstruct staff and patient movement. This observation allowed for an accurate reflection of the pharmacist's activities towards patient care during the CPRA.

Following documentation and observation by the auditor, an informal educational discussion with the pharmacist was undertaken to discuss any identified deficiencies related to patient safety. The deficiencies were discussed in the form of a situational analysis, with CAPAs suggested to address the deficiencies and an agreement reached between the pharmacist and the auditor for the CAPAs. The identified deficiencies related to patient safety were presented as case studies.

The CPRA was concluded through signing the audit tool by the pharmacist (section E) and by the two auditors (section G). One of the completed audit tools was given to the pharmacist and the other was kept by the auditors.

2.8.3.3 Educational approach

An innovative educational approach was implemented throughout the CPRAs, during documentation and observation, with emphasis on the assessment of the pharmaceutical care service provided. Figure 2.2 shows the educational approach implemented in the CPRA process.

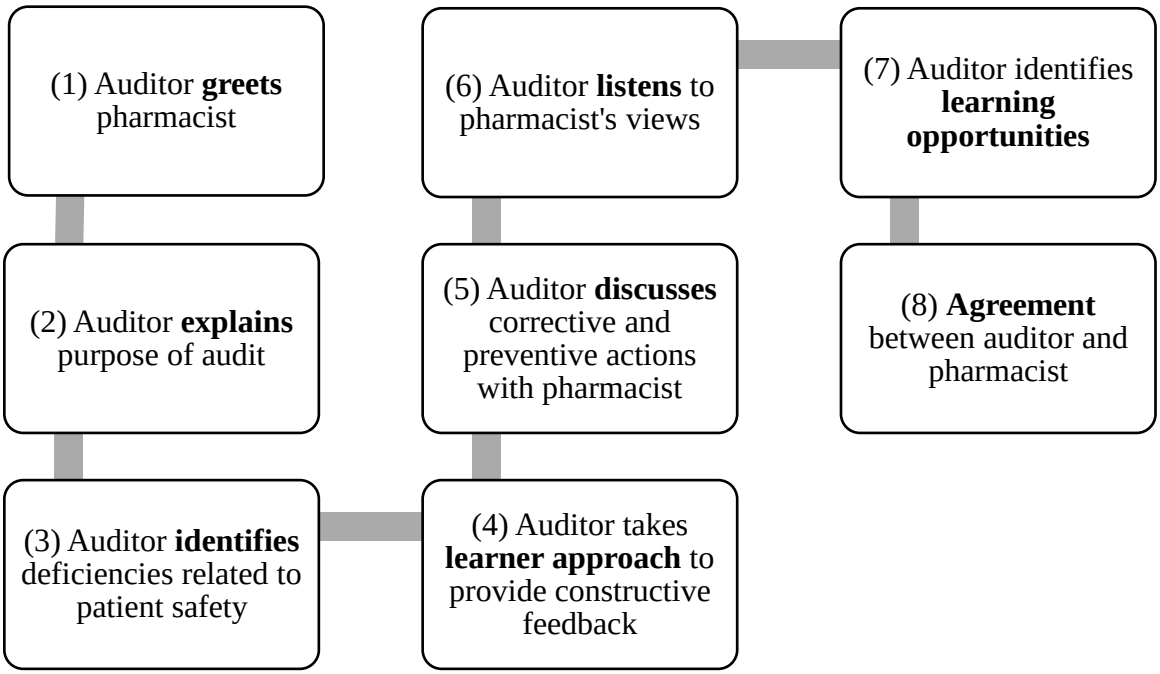


Figure 2.2: Educational approach implemented in the CPRA

Upon arrival at the pharmacy the auditor greeted the pharmacist positively and explained the purpose of the visit. During the on-site fieldwork, deficiencies related to legislation/regulation and patient safety were identified. The auditor took a learner approach and provided views and opinions on the identified deficiencies in a constructive manner. During CPRAs adopting a policing approach, the pharmacists did not interact since the CPRA did not promote interaction. A CPRA with an educational approach encourages the pharmacist to discuss and analyse performance towards patient care. For a CPRA to become educational, an open relationship between the auditor and the pharmacist through listening was promoted. Evaluating the deficiency was at the core of the educational approach. This innovative approach was based on the educational principles that should form the basis of a regulatory audit, such as following the rules of constructive feedback, having a learner-centred and discussion approach, and allowing the pharmacist to express views. Learning opportunities and outcomes that will address

areas of development to enhance performance and improve patient safety were identified. The CPRA was concluded by agreeing on how communication regarding the identified deficiencies between the pharmacist and the auditor would occur. Communication, mainly by electronic mail, between the auditor and the pharmacist was carried out, to ensure that the identified deficiencies were corrected. CAPAs related to patient safety were followed-up by another audit. The CPRA was concluded when CAPAs which were agreed upon were addressed.

2.9 Evaluation of case studies related to patient safety

A case study approach was used to relate the deficiencies identified during the CPRA to patient safety. The case study method of analysis was chosen since it is an in-depth investigation of an activity, event or problem. Case studies are used to help in identifying how the complexities of real-life influence decisions (Crowe et al, 2011).

Each case study was divided into 4 sections namely, case study description, implications to patient safety, educational approach during the audit and CAPAs and follow-up audit (Table 2.3). The first section explains the deficiency identified during the CPRA as the case study description. Implications to patient safety that were identified through the review of literature, medical dossiers, European Public Assessment Reports (EPARs) and consultation with the Marketing Authorisation Holders (MAHs) are included in the second section of the case study. MAHs were especially consulted for deficiencies concerning medicines. These identified implications are presented to analyse and evaluate the impact of the deficiency on patient safety. A list of educational interventions that were carried out by the auditor during the CPRA are included. CAPAs recommended to the

pharmacist by the auditor and agreed upon and findings from the follow-up audit performed to confirm that CAPAs were addressed, are described.

Table 2.3: Case study sections

Section	Section title
1	Case study description
2	Implications to patient safety
3	Educational approach during the audit
4	Corrective and preventive actions and follow-up audit

2.10 Data analysis

Descriptive statistics of the quantitative data collected from the retrospective analysis and from the checklist (section F) during implementation of the tool in CPRAs were undertaken using Microsoft Excel 2016 and presented as bar charts. The qualitative data from the interviews with community pharmacists was analysed and the main features extracted. The deficiencies identified during the observation part of the CPRA were presented as case studies.

Chapter Three

Results

Results of the retrospective analysis of the community pharmacy regulatory audit (CPRA) reports, the interviews with the community pharmacists and implementation of the CPRAs are reported. Identified deficiencies related to patient safety are presented as case studies.

3.1 Results of the retrospective analysis

Five hundred and twelve CPRA reports for a 57-month period (January 2012 to September 2016) were retrospectively analysed, extracting features in the reports that could lead to the lack of identification of patient-related deficiencies.

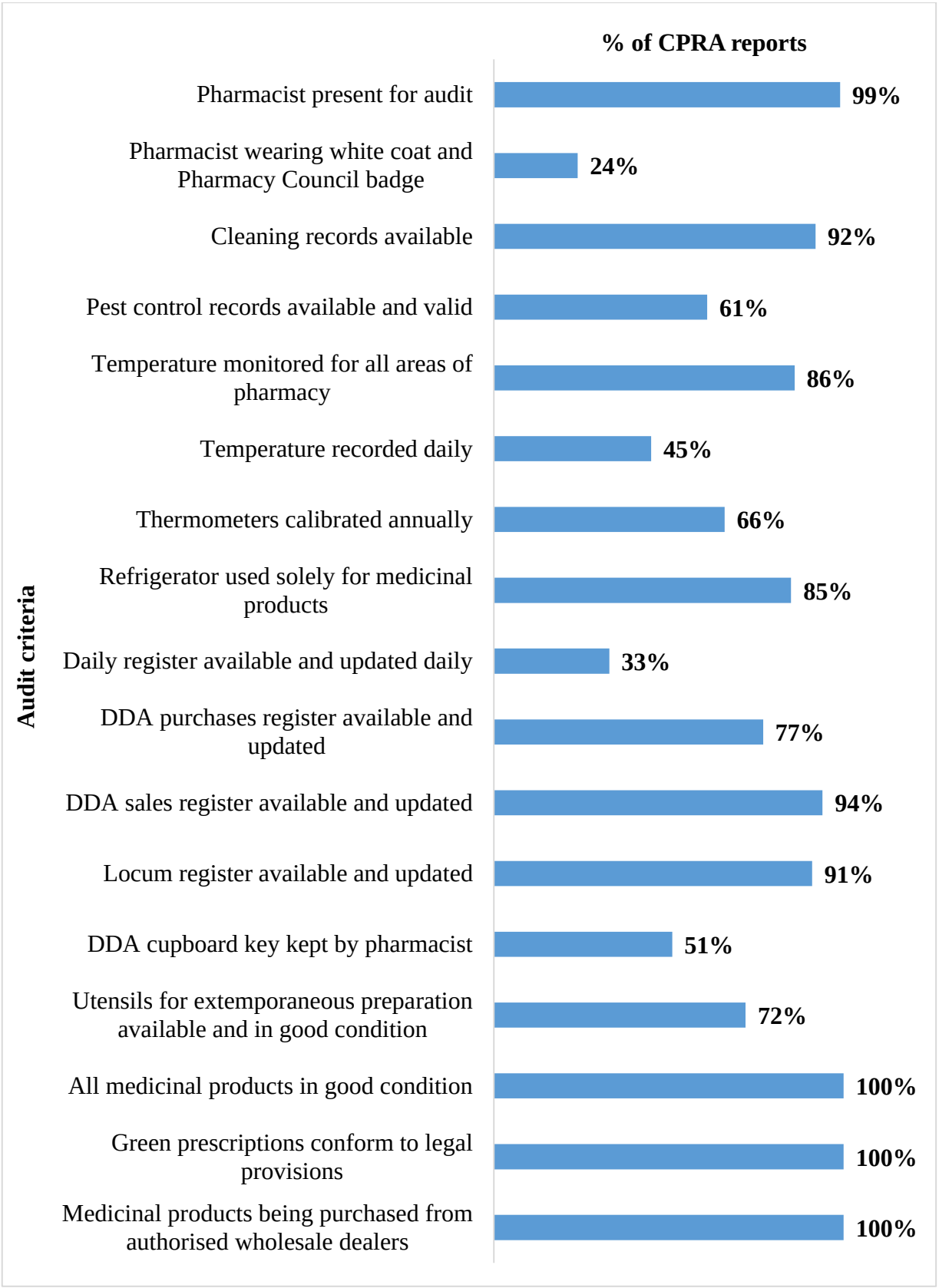
3.1.1 CPRA findings from the retrospective analysis

Out of the 512 CPRA reports analysed, 37 were excluded since they were not complete. Hence, results of 475 complete CPRA reports were included in the analysis.

Two reports indicated that no pharmacist was present at the time of the CPRA. Seventy-six percent (n=361) of the CPRA reports indicated that the pharmacist was not wearing a white coat and the pharmacy council badge whilst attending to professional duties in the pharmacy. Registers and records were reported as not available or not updated as follows: Daily register (67%, n=317), temperature records (55%, n=263), dangerous drugs sales register (23%, n=108), locum register (9%, n=43), cleaning records (8%, n=36), and dangerous drugs purchases register (6%, n=27). Fourteen percent (n=68) of the CPRA reports indicated that temperature monitoring of the pharmacy, store and/or refrigerator

was not being performed. A pest control certificate was not available or was expired in 39% (n=186) of the CPRA reports analysed. Thermometers were not calibrated in 34% (n=162) of the CPRA reports and the refrigerator was not being used solely for the storage of medicines in 15% (n=71) of the CPRA reports.

Forty-nine percent (n=232) of the reports indicated a deficiency regarding the dangerous drugs cupboard namely; the key is left hanging in the lock (n=211), the cupboard is not lockable (n=13), or the cupboard has a lock installed but the key is not available (n=8). For extemporaneous preparations, 28% (n=133) of the CPRA reports indicated that pharmacies had missing utensils; glass slab (n=32), spatula (n=21), pestle and mortar (n=15), graduated cylinder (n=13) or balance (n=9); had a non-graduated cylinder (n=53); a non-functioning electronic balance (n=23); or broken utensils (n=17). All the CPRA reports indicated that the pharmacies had medicines stored in good condition, green prescriptions that conformed to provisions required by law and medicines being purchased from authorised wholesale dealers (Figure 3.1).

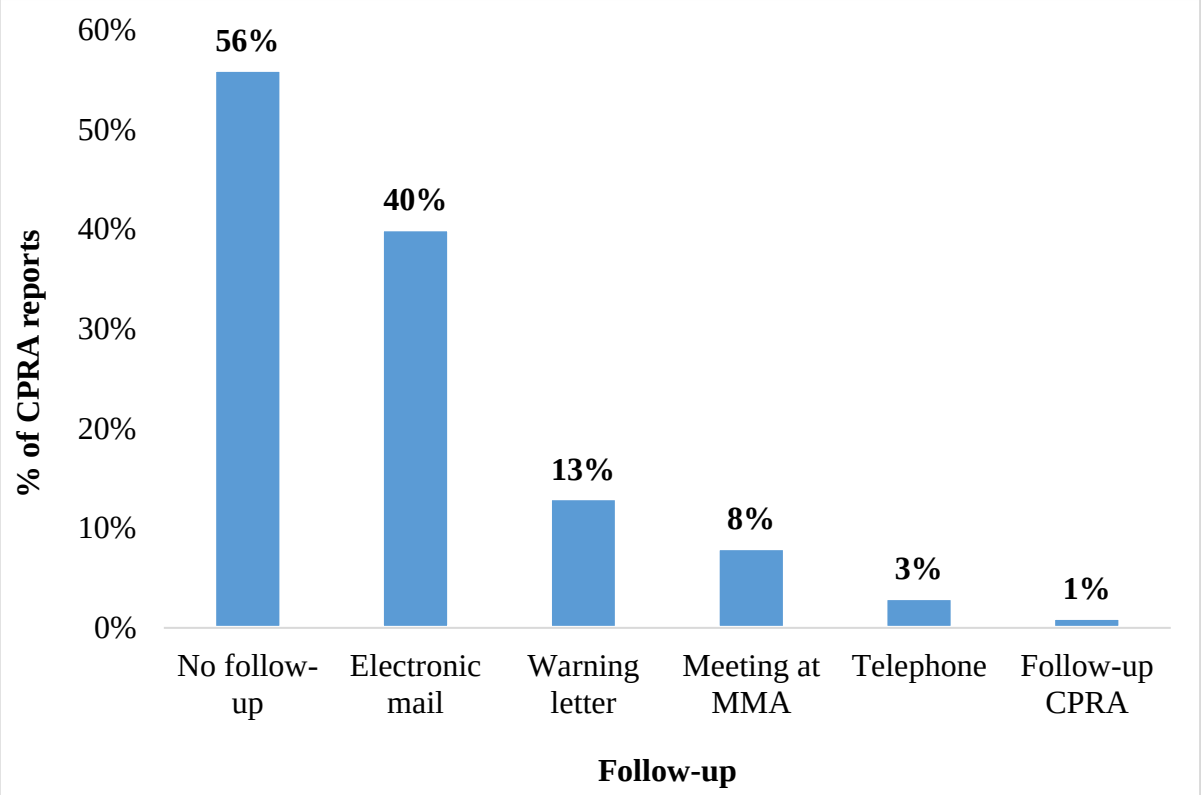


DDA: Dangerous drugs

Figure 3.1: Findings from the retrospective analysis (N=475)

3.1.2 Post-CPRA follow-up in the retrospective analysis

From the retrospective analysis it was noted that corrective actions for the identified findings were either not followed-up or followed-up in five different ways (via telephone, electronic mail, follow-up audit, meeting at the Malta Medicines Authority (MMA) or issue of a warning letter). More than one follow-up method could have been used for each CPRA. Fifty-six percent (n=287) of the CPRA reports assessed reported no follow-up. In 68% (n=194) of these reports, findings were reported but were not followed-up and 32% (n=93) of the reports indicated no findings, hence no follow-up was required. Follow-up by electronic mail was the most prevalent method of follow-up (40%, n=205) (Figure 3.2).



CPRA: Community Pharmacy Regulatory Audit; MMA: Malta Medicines Authority

Figure 3.2: Representation of CPRA follow-up from the retrospective analysis (N=512)

3.2 Results from the interviews with the community pharmacists

Feedback from the interviews with the twelve community pharmacists was classified into: 1) limitations of the CPRA and 2) improvements to the CPRA to ensure patient safety and to enhance professional pharmacy services (Table 3.1).

Nine pharmacists were concerned with pharmacists dispensing Prescription-Only-Medicines (POMs) without a prescription. They stated that dispensing POMs must be regulated and highlighted the need for more discussions on the implementation of pharmacist prescribing. Four pharmacists were concerned with patients being attended to by non-pharmacist staff rather than by the pharmacist (Table 3.1).

All pharmacists stated that the CPRAs do not assess the time spent on a daily basis with the patient providing pharmaceutical care. Eleven pharmacists claimed that the CPRA only focuses on whether the registers are being kept updated. Ten pharmacists perceive the CPRA as a cause of emotional stress due to the risk of being issued with a warning letter implying bad practice. Pharmacists who previously received a warning letter (n=3) stated that this action demotivated them towards providing the best pharmaceutical care to patients since they felt that their interventions were not satisfactory for the MMA since CPRAs only assess compliance to regulation and legislation rather than performance of pharmaceutical care (Table 3.1).

Table 3.1: Key feedback from interviews with the community pharmacists (N=12)

Limitations of the CPRA	**Improvements to the CPRA to ensure patient safety and to enhance professional pharmacy activities**
Does not assess time spent providing pharmaceutical care to patients (n=12)	Ensure dispensing of Prescription-Only-Medicines (POMs) with a prescription (n=9)
Focus is only on registers (n=11)	Ensure patients requesting medicines or advice are attended to by pharmacist and not by non-pharmacist staff (n=4)
Issue of warning letters (n=10)	Ensure actual temperature monitoring to prevent falsified temperature records (n=3)
No training of pharmacists and other staff regarding what is expected by the MMA during the CPRA (n=7)	Ensure internet access in each pharmacy to check for drug interactions and adverse drug reactions (n=3)
Focus is on extemporaneous utensils, where preparation of extemporaneous medicines is nowadays rarely carried out in community pharmacy (n=3)	Identify medication errors and implement an adverse drug reaction reporting system (n=2)
Policing-approach by the MMA auditors during the CPRA (n=2)	Implement SOPs in community pharmacies (n=1)
	Standardise point of care testing services in pharmacies (n=1)
	Ensure presence of health and safety measures at the pharmacy premises (n=1)

3.3 Results of the CPRA implementation

A total of 104 audits were carried out from January to November 2017. Ninety-four audits were included namely; renewal audits (n=81), follow-up audits type b (n=9) and spot-check audits (n=4). Follow-up audits type b did not entail use of the CPRA tool since these audits were carried out to verify concordance following the CPRA. Follow-up audits (n=7) were carried out to assess whether the identified deficiencies related to patient safety were addressed and are presented in the case studies. Variation audits (n=6) and follow-up audits type a (n=4) were excluded due to their administrative nature and lack of patient-related observations. A total of 85 CPRAs using the audit tool were carried out by the researcher; 81 renewal audits and 4 spot-check audits (Figure 3.3).

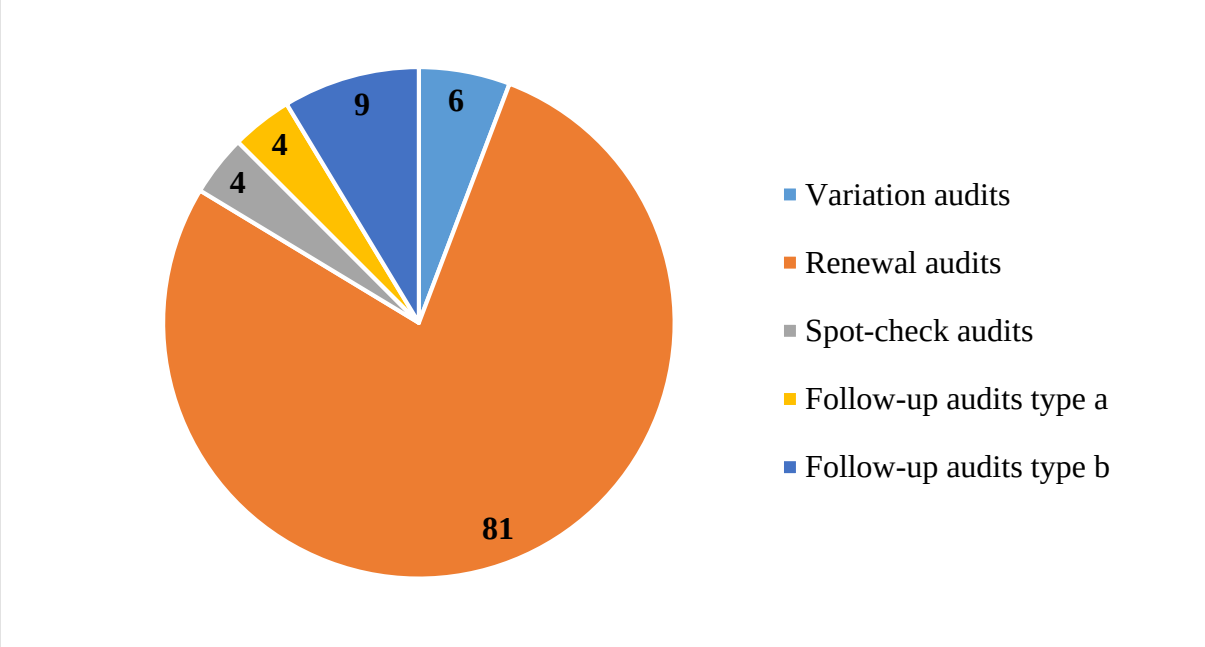


Figure 3.3: Representation of the different types of CPRAs (January-November 2017) (N=104)

The estimated time taken for each renewal and spot-check audit ranged between 60 to 80 minutes and follow-up audits took between 25 to 35 minutes. This estimated time excludes preparation time, travelling, compilation of the report and communication (Table 3.2).

Table 3.2: Estimated time for renewal, spot-check and follow-up audits (N=94)

	Estimated time taken (minutes)	
Type of audit	***Range***	***Median***
Renewal (n=81)/ **Spot-check** (n=4)	60-80	70
Follow-up (n=9)	25-35	30

Sixty-two pharmacists present at the time of the CPRA were managing pharmacists.

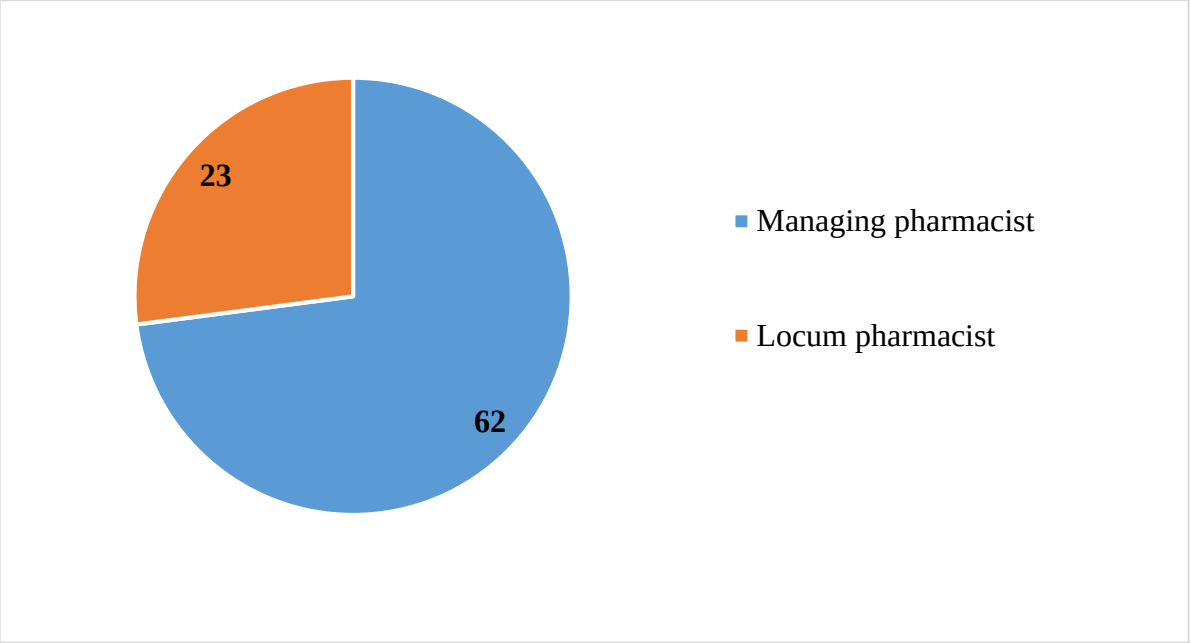


Figure 3.4: Pharmacist present at time of CPRA (N=85)

3.3.1 Findings from CPRA implementation

This section presents the identified findings relating to implementation of the checklist (section F) of the CPRA tool. The results are represented as ‘yes’ and ‘no’, where a ‘yes’ implies conformance and a ‘no’ implies identification of a deficiency.

SOPs were available and being used in only 5 out of the 85 pharmacies. In 81 pharmacies, all POM medicines were stored behind the counter, while in 4 pharmacies inhalers, such as ipratropium, budesonide and salbutamol, high-dose codeine containing medicines and hormonal preparations, such as oral contraceptives, were stored on the side of the counter and easily accessible by patients. Sixty-nine pharmacies were using the refrigerator solely for medicines, while in 16 pharmacies food and drinks were also stored. In 79 pharmacies all medicines were stored in the refrigerator in good condition, unspoiled and non-expired, while in 6 pharmacies spoiled boxes due to water, medicines with frost at the back of the fridge, or expired stock not separated from non-expired stock were observed. Refrigerators in 83 pharmacies were of adequate capacity, while in 2 pharmacies refrigerators were too small to accommodate the volume of medicines required for daily pharmacy services.

With regards to thermometer calibration and air conditioner servicing certificates, 53 and 3 pharmacies respectively, had valid certificates available. Out of the 82 pharmacies with no air conditioner certification available, 63 pharmacists stated the air conditioner is serviced annually, however no receipt of service is kept, while 20 pharmacists stated that the air conditioner is never serviced. Monitoring and recording of maximum and minimum (max/min) refrigerator temperatures for pharmacy stock (n=64) and POYC

stock (n=66), and room temperature of pharmacy stock (n=68) and POYC stock (n=65), were being performed on a daily basis. For the other pharmacies no records were available (n=23), or temperatures were not being recorded daily (n=54). All (n=85) pharmacies had an expiry date management system in place.

In all (n=85) pharmacies a pharmacist was present at the pharmacy for the CPRA. The locum register was complete in 48 pharmacies. Thirty-seven pharmacies did not have a locum register available. Forty-one pharmacists were wearing their pharmacy council badge and 23 pharmacists were wearing a white coat at the time of the CPRA. In 51 pharmacies, the daily register was kept updated, while in 34 pharmacies the daily register was either not updated (n=33) or not available (n=1). Registers in 23 pharmacies were identified as not filled in correctly. Two pharmacies were not keeping prescriptions on premises.

The dangerous drugs registers for purchases (n=79) and sales (n=58) of pharmacy stock, and for received (n=79) and dispensed (n=46) Pharmacy-Of-Your-Choice (POYC) stock, were available and updated. For the other pharmacies, the registers were either not updated (n=59) or not available (n=19). Seven dangerous drugs sales registers were not in the correct format. No pharmacy had destroyed any expired or unwanted dangerous drugs and the dangerous drugs were being kept by the pharmacy in a segregated area in all pharmacies. Seventy-four pharmacies carry out an annual stock take of dangerous drugs. Four pharmacies were not storing dangerous drugs in a lockable cupboard. Out of the 81 pharmacies that keep dangerous drugs in a lockable cupboard, 25 keep the key in the pharmacist's possession while the other 56 pharmacists either leave the key hanging

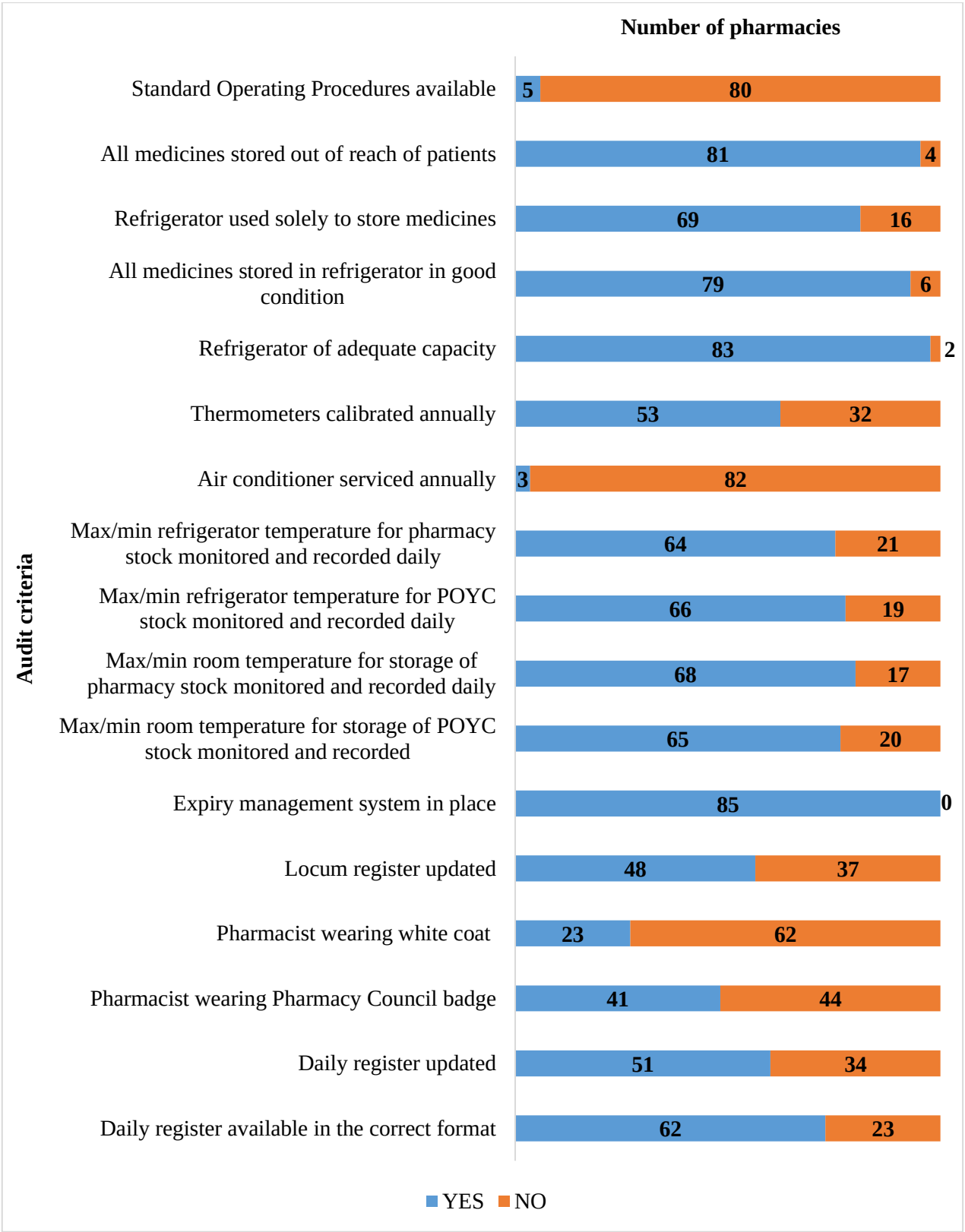
in the lock (n=48) or store it in a drawer at the pharmacy (n=8). Dangerous drugs cupboards in 8 pharmacies were not adequate to permit the orderly storage of all dangerous drugs required for pharmacy services, while in 1 pharmacy it was observed that due to lack of space, a box of diazepam 5mg from the POYC stock was stored outside the cupboard. Expired dangerous drugs were stored in a designated area in 82 pharmacies, while in the other 3 pharmacies expired dangerous drugs were stored outside the dangerous drugs cupboard.

It was observed that 38 pharmacies prepare extemporaneous preparations. All these pharmacies had labels, a dedicated area and all the utensils required for extemporaneous preparation. All pharmacies, irrespective of whether or not they prepare extemporaneous preparations, should have graduated cylinders and tablet counters available. However, 9 pharmacies did not have graduated cylinders and were using non-graduated cylinders or disposable syringes, while 5 pharmacies did not have a tablet counter.

Regarding pharmacy premises, security arrangements were in place for 73 pharmacies. External and internal fixtures were in a good state of repair in 82 pharmacies. Two pharmacies had boxes full of stock obstructing the entrance to the pharmacy. One pharmacy had no sign affixed to the door of the pharmacy and the sign was illegible in 2 pharmacies. The dispensing bench was full of clutter and boxes in 13 pharmacies. All pharmacies (n=85) were equipped with potable water, toilets and restricted access behind the counter to confidential information. One pharmacy did not have adequate lighting. Seventy-four pharmacies were clean, while 11 showed signs of uncleanliness, such as

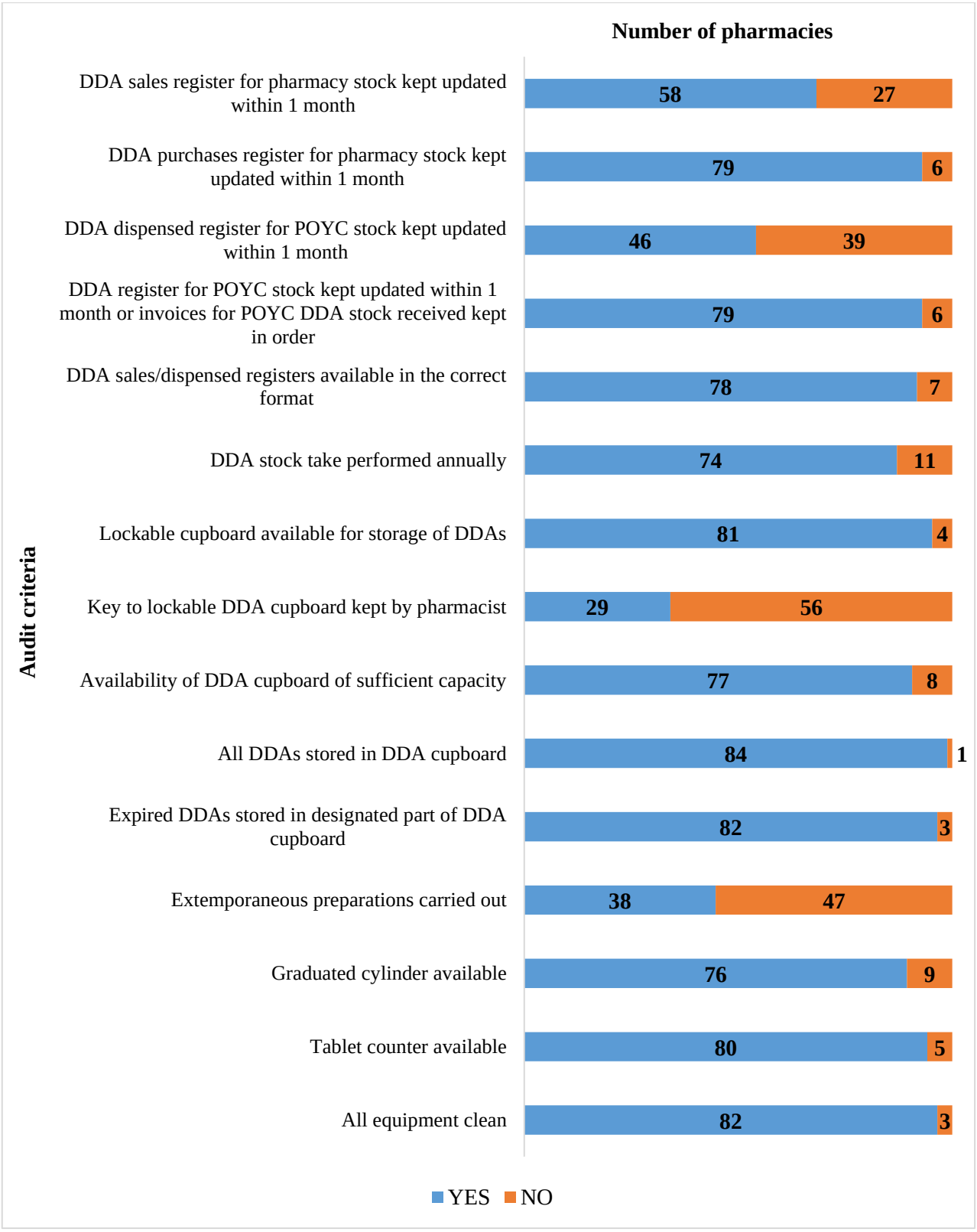
excessive dust on shelves. All pharmacies (n=85) carry out pest control, however only 43 pharmacies had non-expired and valid certificates.

The British National Formulary was available in 79 pharmacies as a reference book. All pharmacies (n=85) were equipped with internet access. The pharmacies that did not have a British National Formulary stated that they search online to respond to patient queries. A sharps bin was not available in 3 pharmacies. All pharmacies (n=85) had a dedicated area for expired medicines which was labelled in 78 pharmacies.



Max/min: maximum/ minimum; POYC: Pharmacy-Of-Your-Choice

Figure 3.5a: Findings from the implementation of CPRAs (January-November 2017) (N=85) (1)



DDA: Dangerous drugs; POYC: Pharmacy-Of-Your-Choice

Figure 3.5b: Findings from the implementation of CPRAs (January-November 2017) (N=85) (2)

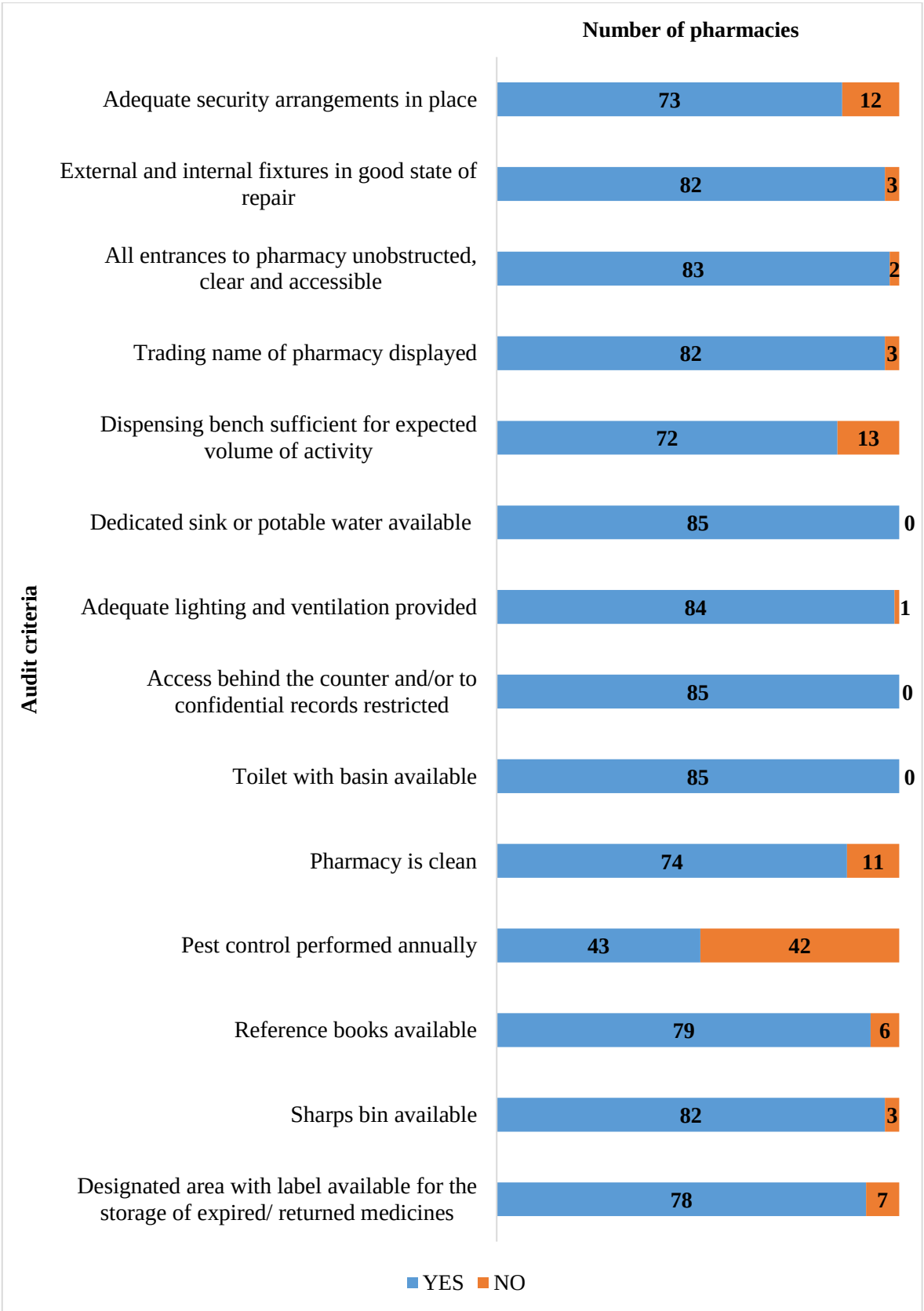


Figure 3.5c: Findings from the implementation of CPRAs (January-November 2017) (N=85) (3)

3.4 Case studies on the identified deficiencies related to patient safety

The 7 case studies related to patient safety evaluated were: Dispensing problems (n=4), inventory deficiencies (n=2) and inequity of treatment (n=1) (Table 3.4).

Table 3.3: Case studies evaluated (N=7)

Dispensing problems (n=4)	• Dispensing error of methotrexate 2.5mg instead of methyldopa 250mg • Near-miss medication error • Dispensing a POM without a prescription • Filling of POYC prescriptions by non-pharmacist staff
Inventory deficiencies (n=2)	• Expired vaccines • Inappropriate storage temperature: Refrigerator temperature below 2°C
Inequity of treatment (n=1)	Inequity of treatment between private and government-sponsored patients

The case studies evaluated exemplify how the educational approach was incorporated in the CPRAs to address identified deficiencies related to patient safety. The analysis of each case study is presented as implications of the identified deficiency to patient safety which could negatively impact patient care outcomes. Six case studies were identified during the CPRAs, while one case study was a reported complaint. Educational interventions (N=44) were implemented during the informal educational discussions between the auditor and the pharmacist, and CAPAs (N=46) for the identified deficiencies were identified and followed-up during the follow-up CPRAs, one for each case, to ensure that concordance was reached in the interest of patient safety (Table 3.4).

Table 3.4: Educational interventions and corrective and preventive actions for the case studies

	Case Study	Educational interventions (N=44)	Corrective and preventive actions (N=46)
1	Dispensing error of methotrexate 2.5mg instead of methyldopa 250mg	**5**	**7**
2	Near-miss medication error	**5**	**3**
3	Dispensing a POM without a prescription	**6**	**7**
4	Filling of POYC prescriptions by non-pharmacist staff	**6**	**6**
5	Expired vaccines	**7**	**8**
6	Inappropriate storage temperature: Refrigerator temperature below 2°C	**9**	**11**
7	Inequity of treatment between private and government-sponsored patients	**6**	**4**

3.4.1 Case study 1: A dispensing error of methotrexate 2.5mg instead of methyldopa 250mg

A complaint was reported to the MMA regarding a dispensing error of methotrexate 2.5mg instead of methyldopa 250mg. The patient presented to a particular pharmacy with a POYC prescription for iron supplementation, enalapril 5mg and methyldopa 250mg. The patient left the POYC documents at the pharmacy and collected the medicines when instructed by the pharmacist. At home, the patient noted that the size of the methyldopa tablets was different from that normally dispensed, however since the patient was illiterate and both methotrexate and methyldopa are yellow and oval shaped, the patient still took the medicine without going back to the pharmacy or physician to query the observed difference. After 3 days of taking methotrexate therapy instead of methyldopa, the patient developed a rash on the lower abdomen, and following consultation with a general practitioner, the patient was prescribed and dispensed hydrocortisone cream. The rash did not resolve and continued to spread over the body and oral pain also developed. Following consultation with a dentist, the patient was prescribed co-amoxiclav 1g. The abdominal rash and oral pain worsened and the patient visited the emergency department at Mater Dei Hospital. The patient was asked by the emergency physician to indicate the drugs being taken and the patient showed the list of medicines to the physician. The dispensing error was identified at the emergency department, where the patient was referred for further tests by a consultant haematologist and an infectious disease specialist.

The auditor (researcher) carried out a spot-check audit after this reported complaint to discuss with and listen to the managing pharmacist, understand the possible cause/s of this unfortunate dispensing incident and explain how similar recurrences could be prevented. The pharmacist explained the incident to the auditor from receipt of the prescription from the patient at the pharmacy to when the incorrect medicine was dispensed. The pharmacist explained that the prescription and the documents required to process POYC medicines are received one week prior to the date of dispensing. The pharmacist claimed that for POYC medicines a non-pharmacist employee inputs the quantity of the prescribed medicines according to the physician's prescription into the computerised POYC system and issues the label. The pharmacist on duty packs the medicines according to the label affixed to the documents. Upon discussion between the auditor and the managing pharmacist it was noted that when the patient presents for collection of POYC medicines, dispensing is carried out by a pharmacist without re-checking of the medicines and quantities.

The managing pharmacist showed the auditor where methotrexate 2.5mg and methyldopa 250mg are stored. It was observed that these medicines are stored next to each other alphabetically and are both supplied by the POYC department in blister packs and not in the original outer packaging. The pharmacist stated that the patient did not come to the pharmacy to query any difference between the previous medicine and the one dispensed, and that at no time did the general practitioner or dentist, who allegedly treated the patient, query the medicines being taken by the patient. The pharmacist expected the patient to notice any difference in medicines and stated that the patient should have returned to the pharmacy to ask questions. The pharmacist stated that the packaging of POYC medicines changes regularly and that most patients often query whether a medicine with a different

trade name and/or different outer packaging is the same as the previous medicine the patient was taking.

3.4.1.1 Implications to patient safety

Methotrexate is an effective and safe treatment when taken as indicated once weekly, however it can have serious consequences, which can be fatal, if taken as a daily dose instead of a weekly dose. Clinical manifestations of toxicity may include; nausea, vomiting, diarrhoea, mucositis, stomatitis, oesophagitis, elevated hepatic enzymes, renal failure, rash, myelosuppression (leukopenia, pancytopenia, thrombocytopenia), acute lung injury, tachycardia, hypotension, and neurologic dysfunction (depression, headache, seizures, motor dysfunction, stroke-like symptoms, encephalopathy, coma) (Moore et al, 2004; Howard et al, 2016). Toxicity manifestations can have an early onset within 1 month of treatment or a late onset (Arnet et al, 2011).

In this case, the patient was prescribed methyldopa 250mg once daily to treat hypertension, however ended up taking methotrexate 2.5mg daily due to the dispensing error. The patient developed signs of methotrexate toxicity namely a rash on the lower abdomen, which did not resolve with steroid treatment and which spread all over the body, and oral pain, likely mucositis, due to the antifolate effect of methotrexate, which did not resolve with antibacterial treatment. Methotrexate toxicity was evident in this case due to the incorrectly dispensed methotrexate instead of methyldopa which led to side-effects and need for daily treatment with folic acid (additional drug for the patient) after the incident was identified.

3.4.1.2 Educational approach during the audit

Following an informal educational discussion with the managing pharmacist during the complaint-driven audit, the auditor carried out 5 educational interventions:

(1) The auditor explained that non-pharmacist staff are allowed to prepare medicines, however the pharmacist must always check both the prescription and the POYC label affixed to the prescription issued by the non-pharmacist to confirm correctness at the time of dispensing and should confirm medicine indication and dosage with the patient at the time of dispensing.

(2) The auditor highlighted that the pharmacist is responsible to ensure that the medicine dispensed is correct and should not expect the patient to notice any differences.

(3) Methotrexate and methyldopa are both supplied in blister packs and not in their original outer packaging and this similarity in packaging should be taken into consideration when placing these medicines on shelves. Suggestions by the auditor were made, such as devising methods of alert e.g. use of separators and highlighting the risks of cytotoxics.

(4) The auditor advised the pharmacist regarding storage of 'written-alike', 'look-alike' and 'sound-alike' medicines. In this case methotrexate and methyldopa, both start with 'meth', therefore care should be taken to separate these medicines. Other medicines with same generic name and dosage form but with a different dose, such as valsartan 80mg and 160mg, should also be highlighted to avoid picking up the wrong dose whilst dispensing.

(5) The auditor explained the need to explore the possibility to employ a new POYC system to avoid accumulation of POYC documents at the pharmacy for 1 week, reducing the risk of mix-up of documents and in turn decreasing the risk for dispensing errors.

The auditor and the managing pharmacist agreed that CAPAs will be implemented to prevent future dispensing errors and to improve pharmacy practice at the pharmacy in the interest of patient safety.

3.4.1.3 Follow-up audit and corrective and preventive actions

A follow-up audit was performed 8 weeks after the complaint-driven audit. CAPAs (n=7) were implemented by the managing pharmacist to ensure patient safety following the educational discussion with the auditor.

- The managing pharmacist confirmed that although POYC medicines are still prepared by a non-pharmacist, double-checking with the prescription is always being carried out by a pharmacist before dispensing. A full-time pharmacist position is being considered to prepare POYC medicines.
- All POYC cytotoxic medicines are stored alphabetically in a labelled, separate cupboard to alert the pharmacist when dispensing these medicines.
- All medicines are being stored alphabetically with the label facing forward.
- Shelves were labelled and separators were installed as a partition between medicines for all medicines in the pharmacy to prevent dispensing errors.
- Labels to highlight generic name were affixed to ‘sound-alike’, ‘look-alike’ and ‘written-alike’ medicines, even for same generic name with different doses, e.g. hydralazine and hydroxyzine, enalapril 5mg and 20mg, atorvastatin 10mg, 20mg and 40mg, amitriptyline 10mg and 25mg, amongst others. This was carried out to alert pharmacy staff to the need for double-checking when picking these medicines from the shelves.

- POYC medicine stock-take will be performed every 2 months to account for any stock discrepancies.
- A new POYC system was implemented, where a patient prescribed a small number of medicines (≤ 3 medicines) will be served on the same day, while longer orders (≥ 4 medicines) will be served within 1 or 2 days.

Concordance was reached between the managing pharmacist and the auditor which was confirmed by the follow-up audit to safeguard the patient and the pharmacy profession.

3.4.1.4 Methotrexate dispensing error focus group

Since this identified deficiency was the first reported case to the MMA related to a methotrexate dispensing error which threatened patient safety, a focus group was set-up to discuss this particular case after the follow-up audit. The focus group consisted of the Director of the Inspectorate and Enforcement Directorate (IED) at the MMA, two auditors from the MMA and 3 community pharmacists. The case was discussed without disclosing the identity of the community pharmacy and pharmacist. Root causes for dispensing errors were noted, including the cause of this particular case, as well as recommendations which could be implemented to prevent such errors. Seven possible root causes for errors and 18 recommendations to prevent such errors were identified during the focus group (Table 3.5).

Table 3.5: Possible root causes for dispensing errors and recommendations discussed in focus group

Possible root cause for errors (N=7)	Recommendations (N=18)
Look-alike, sound-alike and written-alike medicines	• Should be taken into consideration when issuing medical tenders by the Central Procurement and Supplies Unit • Labelling of shelves • Use of separators • Use of reminders/alert pop-ups in the POYC computer system when processing prescription to alert staff about these drug names which may be confused
Dispensing errors at counter level	• Dispensing to always be carried out by a pharmacist • A pharmacy technician can prepare the medicines according to the prescription, but should never dispense without consultation with a pharmacist • Medicines should be rechecked before dispensed to the patient and clarified with the patient by showing the medicines to the patient at the time of dispensing • Organising dispensing benches to be free from clutter • Reducing workload and stress at the workplace, e.g. a maximum quota of patients can be suggested per pharmacy/pharmacist/pharmacy technician employed/present at the pharmacy • Thorough patient counselling is important to detect any dispensing error before medicine is dispensed
Dangers of cytotoxic drugs	Cytotoxic drugs should be stored in a manner which alerts the pharmacist and with additional safety considerations e.g. enclosing them in plastic bags or glass containers, use of alert pop-ups on computer system, storage in separate area/cupboard

Possible root cause for errors (N=7)	Recommendations (N=18)
Inadequate identification and reporting of medication errors	A reporting system can be implemented, where the pharmacist can report any dispensing errors as they occur; the system should be consequences-free i.e. not resulting in consequences or breach of law so as to encourage reporting without any fear of reprisal
Storage of loose blister packs - risk of picking up the wrong blister pack	Loose blister packs should never be dispensed; appropriate packaging, patient information leaflets and labelling must always be supplied to patients; this should be implemented by the Central Procurement and Supplies Unit at POYC level and at individual pharmacy level
Accumulation of patient files at pharmacy	• To prepare POYC medicines at the time of receipt of documents • To keep patient files for a maximum of 2 days and not for 1 week
Illegible prescriptions *(Not applicable to this case)*	• Use of electronic prescriptions • Confirm that prescription is legible and correct. Pharmacist should not dispense if illegible and clarification from physician should be sought • Any clarification from physician should be documented promptly

3.4.2 Case study 2: Near-miss medication error

During a CPRA the auditor observed a deficiency whereby a non-pharmacist dispensed a prescription without consulting with the pharmacist and without patient counselling, resulting in a near-miss medication error. An elderly patient presented at the pharmacy with a prescription for clarithromycin 500mg. The non-pharmacist attended to the patient, checked the prescription, prepared the medicine and dispensed it to the patient. The auditor identified the deficiency of a non-pharmacist dispensing a medicine without confirming the prescription with the pharmacist and without providing any patient counselling, and brought it to the attention of the pharmacist during the CPRA. The pharmacist immediately attended to the patient who was leaving the pharmacy and checked the prescription. The pharmacist confirmed that the correct medicine was dispensed according to the prescription. The pharmacist queried the patient's medication history and noted that the patient is concomitantly taking simvastatin 40mg daily. The pharmacist advised the patient to stop the simvastatin for 7 days whilst taking clarithromycin due to a potential major drug-drug interaction and to restart the simvastatin when the antibiotic course is finished. This situation, which occurred during the CPRA, made the pharmacist feel extremely concerned about this deficiency and the pharmacist wanted to ensure that this near-miss would not recur. The auditor's intervention led to the pharmacist correcting the error during the CPRA to avoid a near-miss medication error.

3.4.2.1 Implications to patient safety

A potential major drug-drug interaction exists between simvastatin and clarithromycin (Lee et al, 2001; Li et al, 2014) and concomitant therapy is contraindicated (British National Formulary, 2017). Clarithromycin is a potent inhibitor of the cytochrome P3A4 enzyme, which is the same major enzyme responsible for the metabolism of simvastatin. High serum simvastatin concentrations, which can result due to alteration of the pharmacokinetics of simvastatin by clarithromycin, increase the risk of simvastatin toxicity (Li et al, 2014). The interaction of statins (simvastatin) with macrolide antibiotics (clarithromycin) may result in myopathy, rhabdomyolysis, hyperkalaemia and acute kidney injury (Lee et al, 2001; Fallah et al, 2013). If this case was not brought to the attention of the pharmacist by the auditor, patient safety may have been threatened due to the increase in simvastatin concentration by clarithromycin. The co-prescription of simvastatin and clarithromycin may also lead to hospitalisation, especially in the elderly, due to risk of hyperkalaemia and acute kidney injury (Li et al, 2014).

3.4.2.2 Educational approach during the audit

Following an informal educational discussion with the pharmacist during the audit, the auditor performed 5 educational interventions:

(1) The pharmacist's concern regarding the situation was acknowledged and the auditor explained to the pharmacist that errors in day-to-day pharmacy practice do occur, however, as in this case, identifying the error and ensuring appropriate CAPAs is key to safeguard patient safety.
(2) The auditor suggested documenting similar errors since learning from near-miss errors helps to minimise the risk of future errors.

(3) The auditor stressed the importance of dispensing to always be carried out by a pharmacist. Non-pharmacist staff can assist in preparing medicines but dispensing should always be carried out by a pharmacist or under the direct supervision of a pharmacist.

(4) The auditor highlighted that dispensing errors and other threats to patient safety are the responsibility of the pharmacist on duty and not of non-pharmacist staff.

(5) The auditor explained that overseeing all activities performed by non-pharmacist staff is not possible, however offering the appropriate training to non-pharmacist staff is important to ensure patient safety in practice e.g. training regarding situations when to refer patients to the pharmacist.

The auditor and the pharmacist agreed that CAPAs will be implemented to minimise the risk of similar near-miss dispensing errors and to enhance pharmacy practice at the pharmacy to improve patient safety.

3.4.2.3 Follow-up audit and corrective and preventive actions

A follow-up audit was performed after 8 weeks. CAPAs (n=3) were implemented to promote patient safety following the educational discussion between the auditor and the pharmacist:

- A SOP for referral of patients to the pharmacist for ailments involving medicine dispensing was developed.

- Training was given to non-pharmacist staff by the pharmacist with regards to referral of patients to the pharmacist for ailments requiring medicine dispensing and training records were made available.
- A ‘near-miss medication error’ log was developed as an error management system to facilitate identification of any patterns with regards to similar errors. The log includes details of near-miss medication errors, patient details, contributing factors and corrective actions taken. An observed recorded near-miss error included choosing the wrong dose of rosuvastatin (15mg instead of 5mg) and the corrective action was labelling of the shelves for same generic name with different doses to alert staff when preparing and dispensing medicines.

Concordance was reached between the pharmacist and the auditor, which was confirmed by the follow-up audit, to prevent future near-miss medication errors in the interest of patient safety.

3.4.3 Case study 3: Dispensing a Prescription-Only-Medicine without a prescription

During a CPRA the auditor observed a deficiency related to patient safety when a pharmacist dispensed a POM (isotretinoin) without being presented with a prescription by the patient. A 20-30-year-old female patient presented at the pharmacy asking for isotretinoin 20mg for acne without a prescription. The pharmacist dispensed isotretinoin 20mg according to the patient's request. A prescription was not presented throughout the whole process of dispensing and the pharmacist did not ask for a prescription. The pharmacist did not educate the patient about the need for a prescription for isotretinoin and regarding the use of effective contraception with isotretinoin therapy. The auditor brought this deficiency related to patient safety to the attention of the pharmacist and explained that since isotretinoin is a POM, it and other POMs, should not to be dispensed without a prescription. The auditor engaged in an educational discussion with the pharmacist. The pharmacist stated that the patient presents at the pharmacy every month for isotretinoin, hence the reason for not asking for a prescription. The pharmacist stated that many regular patients often ask for chronic medications without a prescription, such as for levothyroxine, duloxetine and omeprazole. The pharmacist was concerned regarding the dispensing of POMs without a prescription after this situation was highlighted by the auditor.

3.4.3.1 Implications to patient safety

All retinoids are teratogenic with an extremely high risk of foetal exposure resulting in foetal malformations and life-threatening congenital abnormalities (Meigel, 1997; Rademaker, 2010).[21,22] Due to the high teratogenicity of retinoids, Roche, the Marketing Authorisation Holder of Roaccutane®, launched the 'Pregnancy Prevention Programme' (PPP) in 1988 as a Risk Management Plan (Mitchell et al, 1995; Crijns et al, 2011). This programme was launched as a measure to reduce the risk of birth defects in women of childbearing potential and to increase compliance to reduced-risk prescribing and use.[23,24] The patient, in this case is a 20-30-year-old female, is considered a woman of childbearing potential and is predisposed to the risk of teratogenicity. The risk of foetal exposure to isotretinoin is decreased by use of reliable contraception. An acknowledgement form should be signed by the patient, confirming that the patient is aware of the risks of teratogenicity associated with isotretinoin (Perlman et al, 2001). In this case it is was not known whether the patient is practicing effective and reliable contraceptive methods.

[21] Pharmacovigilance Risk Assessment Committee. PRAC recommends updating measures for pregnancy prevention during retinoid use [Online]. London: European Medicines Agency; 2018 [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Retinoids_31/Recommendation_provided_by_Pharmacovigilance_Risk_Assessment_Committee/WC500243544.pdf

[22] Alliance Pharmaceuticals. Isotretinoin 20mg capsules - Summary of Product Characteristics [Online]. UK: eMC; 2017 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/medicine/15655

[23] Roche. Pharmacist's guide to dispensing Roaccutane® (isotretinoin) [Online]. Ireland: Roche Products Limited; 2016 [cited 2018 May 30]. Available from: URL: http://www.hpra.ie/img/uploaded/swedocuments/Roaccutane_HCP_Pharmacists%20Guide_02.2016-2196313-22082017115143-636389995120468750.pdf

[24] iPledge. The iPLEDGE Program: Pharmacist guide for isotretinoin [Online]. USA: iPledge; 2005 [cited 2018 May 30]. Available from: URL: https://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4311b1-04-addendum-sponsor.pdf

3.4.3.2 Educational approach during the audit

Following an informal educational discussion with the pharmacist, the auditor carried out 6 educational interventions during the CPRA:

(1) The auditor highlighted the importance of dispensing against a prescription for all POMs, especially for high-alert[25] drugs, such as isotretinoin.

(2) The auditor highlighted the risks associated with dispensing isotretinoin without a valid prescription. The patient is a 20-30-year-old female and likely of childbearing potential, hence the risks associated with isotretinoin are greater in this case.

(3) Following intervention by the auditor, the pharmacist was concerned regarding dispensing without a prescription, and the auditor explained that the pharmacist should always consider the risk of dispensing without a prescription versus the risk of leaving the patient without treatment. A risk analysis should be carried out to evaluate each individual case. However, in this case the risk of dispensing without a prescription is higher that the risk of not being treated for acne.

(4) The auditor advised regarding the guide to dispensing isotretinoin, in accordance with the PPP, which can be found in the summary of product characteristics (SPC) of all retinoids, under section 4.4 'Special Warnings and Precaution for Use'. The guide specifies that the patient should practice effective contraception 1 month before starting therapy and for 5 weeks after stopping therapy, pregnancy testing should be carried out every month, follow-up by a physician should be carried out every month, prescription limit is 30 days and validity is 7 days from the date of issue of the prescription, the patient is excluded from blood donation during therapy and for 1 month following discontinuation, and the prescription should not to be dispensed if

[25] Institute for Safe Medication Practices (ISMP). ISMP list of high-alert medications in community/ambulatory healthcare [Online]. UK: ISMP; 2011 [cited 2018 May 30]. Available from: URL: http://www.ismp.org/communityRx/tools/highAlert-community.pdf

not issued by or under the supervision of a specialist if it exceeds 7 days from date of issue and if it is not presented at the pharmacy as a hard copy.

(5) The auditor explained the need for availability of acknowledgement forms for oral and topical retinoid therapy at the pharmacy, which should be signed by the patient being treated with retinoids and the dispensing pharmacist at the time of dispensing.

(6) The auditor explained that a photocopy or a scanned soft copy of the prescription can be kept by the pharmacist for regular patients presenting for repeat POMs.

The auditor and the pharmacist agreed that CAPAs will be implemented to ensure that POMs are dispensed against a prescription to enhance pharmacy practice at the pharmacy in the interest of patient safety.

3.4.3.3 Follow-up audit and corrective and preventive actions

A follow-up audit was performed after 8 weeks. CAPAs (n=7) were implemented to ensure patient safety following the educational discussion between the auditor and the pharmacist during the CPRA:

- The pharmacist contacted the patient and confirmed that the patient is practising effective contraception and excluded the risk of pregnancy.
- The pharmacist explained the high risks associated with treatment of isotretinoin to the patient and the need to present a new prescription as a hard copy every month for isotretinoin to be dispensed.
- The PPP was reviewed by the pharmacist.
- Acknowledgement forms for retinoid therapy were made available at the pharmacy.

- Patients are being advised regarding the need to present a prescription for chronic POM medicines to be dispensed.
- A scanned copy of repeat prescriptions will start to be kept in the pharmacy computer system to avoid, as much as possible, the practice of dispensing without prescriptions.
- The pharmacist explained that when a patient presents at the pharmacy without a prescription, a risk analysis is being carried out to analyse the risk of dispensing without a prescription versus leaving the patient without treatment.

Concordance was reached between the pharmacist and the auditor, which was confirmed by the follow-up audit to ensure that the pharmacist is aware of the risks associated with isotretinoin therapy and the risks of dispensing isotretinoin and other POMs without a prescription.

3.4.4 Case study 4: Filling of prescriptions by non-pharmacist staff

During a CPRA, the auditor observed a deficiency of filling prescriptions by a non-pharmacist, whereby the non-pharmacist dispensed POYC medicines without consulting with the pharmacist. A patient entered the pharmacy with a query regarding POYC medicines. The pharmacist directed the patient to a room in the pharmacy where it was observed that the POYC medicines were prepared and dispensed by a non-pharmacist. During the educational discussion between the auditor and the pharmacist, the pharmacist stated that the non-pharmacist is well-trained to prepare and dispense POYC medicines and in handling errors in the system. The auditor stressed that dispensing of medicines should always be carried out by a pharmacist.

3.4.4.1 Implications to patient safety

It has been reported that almost half of all medicines worldwide are prescribed, dispensed or sold inappropriately (Wubante, 2014). Dispensing is a critical and integral part of the safe use of medicines.[26] The separation of prescribing and dispensing provides a safety mechanism as it ensures independent review of a prescription upon commencement of treatment.[27] The pharmacists are the final link between the use of medicines and the patient (Wubante, 2014). In this case, the pharmacist is not ensuring the safe use of chronic medicines by the patient, and the pharmacist's link in the dispensing process is missing. Dispensing involves both the supply of medicines as required by law, as well as

[26] Kumud K. Farai C, Suryawadi S. Role of dispensers in promoting rational drug use, ensuring good dispensing practice [Online]. Geneva: World Health Organisation; 1996 [cited 2018 May 30]. Available from: URL: http://archives.who.int/PRDUC2004/RDUCD/Session_Guides/role_of_dispensers_in_rational_d.htm

[27] The Pharmacy Guild of Australia. Dispensing your prescription medicine: More than sticking a label on a bottle [Online]. Barton: The pharmacy guild of Australia; 2016 [cited 2018 May 30]. Available from: URL: https://www.guild.org.au/__data/assets/pdf_file/0020/5366/the-dispensing-process.pdf

the clinical interpretation and evaluation of the prescription by the pharmacist. The medicine dispensing process should be systematic to safeguard patient health and safety.

3.4.4.2 Educational approach during the audit

Following an informal educational discussion with the pharmacist, the auditor performed 6 educational interventions during the CPRA:

(1) The auditor explained that the pharmacist should ensure that each patient receives the correct medicine and dose together with counselling.
(2) The auditor advised that non-pharmacists can assist the pharmacist in the dispensing process, however the pharmacist should directly supervise the dispensing process to perform necessary interventions.
(3) Non-pharmacists should be adequately trained not to dispense medicines without consultation with the pharmacist and should always refer patients with queries about medicines to the pharmacist.
(4) The auditor stressed that the POYC scheme is a service that requires pharmacist intervention. POYC patients are usually taking more than one chronic medicine and are elderly, hence predisposed to polypharmacy requiring more checking, monitoring and education.
(5) It was acknowledged that the pharmacist delegates many activities to the non-pharmacist since there is a trusting rapport between them, however the auditor highlighted that any resulting medication errors threatening patient safety are the responsibility of the pharmacist.
(6) The auditor suggested incorporating the POYC service into the main dispensary area and not in a separate room to ensure constant and direct supervision by the pharmacist.

The auditor and the pharmacist agreed that CAPAs will be implemented to ensure that POYC medicines will no longer be dispensed by a non-pharmacist in the interest of patient safety.

3.4.4.3 Follow-up audit and corrective and preventive actions

A follow-up audit was performed after 8 weeks and CAPAs (n=6) were implemented following the educational discussion between the auditor and the pharmacist during the CPRA:

- Modifications in the pharmacy were carried out to move the POYC system and into the same area as storage of private medicines.
- SOPs for POYC system and referral of patients to the pharmacist for ailments requiring medicines were developed.
- Training records were made available with all SOPs.
- A pharmacy technician to be employed to work-out POYC instead of a pharmacy assistant is being considered, however the pharmacist confirmed that the pharmacy technician will be under the direct supervision of the pharmacist for dispensing.
- POYC medicines are being re-checked by the pharmacist on duty prior to dispensing.
- Counselling to POYC patients is being provided as written instructions/ information and verbal counselling prior to dispensing.

Concordance was reached between the pharmacist and the auditor, which was confirmed by the follow-up audit to ensure that the POYC dispensing process is always carried out or supervised by the pharmacist on duty to improve patient safety.

3.4.5 Case study 5: Expired vaccines

During a CPRA, the auditor opened the refrigerator and randomly checked the expiry dates of the medicines in the refrigerator as part of the routine CPRA checking. Upon checking the expiry dates, it was observed that there were 4 expired Hepatitis A and B adult vaccines stored with non-expired medicines in the refrigerator. The vaccines had been expired for 10 months.

3.4.5.1 Implications to patient safety

All licensed vaccines are labelled with the required storage conditions and an expiration date. Vaccines must be stored according to the stipulated requirements to ensure that they maintain their potency and efficacy. Potency and efficacy of vaccines may be lost after the expiration date, losing the ability to provide maximum protection, hence vaccines must not be administered after the expiration date (Capen et al, 2012). The expired Hepatitis A and B adult vaccine in this case is licensed with a shelf life of 24 months in support of stability data as presented in the dossier.[28] When administered within the authorised licensed shelf life, an immune response with regards to Hepatitis A was seen in 94% of subjects after the first dose, in 99.5% of subjects after the second dose and in 100% of subjects after the third dose. With regards to Hepatitis B, an immune response was seen in 71% of subjects after the first dose, in 97% of subjects after the second dose and in 99.7% of subjects after the third dose.[27,29] At the end of the shelf life, the inactivated

[28] European Medicines Agency. Twinrix European Public Assessment Report [Online]. London: European Medicines Agency; 2008 [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_Summary_for_the_public/human/000112/WC500044058.pdf

[29] GlaxoSmithKline. Twinrix adult vaccine - Summary of Product Characteristics [Online]. UK: eMC; 2016 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/medicine/2061

virus reaches the maximum acceptable limit of product degradation.[30] After the expiration date, the Hepatitis A and B virus is subject to quick degradation and the potency and efficacy of the vaccine may be lost. In this case, the vaccines had been expired for 10 months, and were highly likely to be less potent, with an the immune response rate not in accordance with the accepted licensed ranges.[31] If the expired vaccines are dispensed and administered because the pharmacist and the health care practitioner do not check the expiration date, the potency may not be sufficient to protect the patient against the virus, thus increasing the risk of contracting the vaccine-preventable hepatitis A/B infection due to negligence. In the event of dispensing, and eventually administering, an expired vaccine, a risk assessment to decide whether the patient needs to be re-vaccinated must be carried out. Risk assessment should be based on characteristics of the individual patient, number of doses given and on the indication of the vaccine. In this case all individuals taking the expired Hepatitis A and B adult vaccine will have to be revaccinated, with another dose given as soon as possible. The risk of experiencing ADRs from revaccination is minimal compared to the risk of contracting the virus, and any ADRs will be similar to those experienced during the normal vaccination schedule.[30]

[30] European Commission. Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use [Online]. Official Journal of the European Union 2001; L311:67-128 [cited 2018 May 30]. Available from: URL: http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32001L0083&from=EN

[31] Health Protection Agency. Vaccine incident guidance [Online]. London: Health Protection Agency; 2012 [cited 2018 May 30]. Available from: URL: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/326417/Vaccine_Incident_Guidance.pdf

3.4.5.2 Educational approach during the audit

Following an informal educational discussion between the auditor and the pharmacist during the CPRA, the auditor performed 7 educational interventions:

(1) The auditor explained to the pharmacist the need to identify whether any expired Hepatitis A and B adult vaccines were administered to patients. This can be carried out by for example checking fiscal receipts for the last 10 months.

(2) The auditor stressed the need for an effective expiry date monitoring system to identify expired vaccines and to separate them from non-expired vaccines until disposal so as to prevent dispensing of expired, and possibly ineffective, vaccines. This practice should apply for other medicines.

(3) The auditor highlighted the use of the 'First-in, First-out' system, which involves placing medicines with closer expiration dates in front to prevent the dispensing of expired vaccines and medicines.

(4) The auditor suggested implementing an inventory reporting system or checking the inventory on a regular schedule for improved medicine management to reduce the risk of dispensing expired vaccines and medicines, in turn decreasing waste and costs.

(5) The auditor explained that in cases when an expired vaccine is dispensed it is important to act quickly to avoid patient harm. The patient should be contacted and any health care professional involved should also be informed. A risk assessment should be carried out if an expired vaccine is administered.

(6) The auditor highlighted the need to always check the expiration date of vaccines and other medicines before dispensing.

(7) The auditor explained how methods of alert can be utilised in cases of expiration dates, such as highlighting medicines using coloured stickers (not only for vaccines) to ensure patients are only supplied with non-expired medicines.

The auditor and the pharmacist agreed that CAPAs will be implemented to ensure that expired vaccines are identified and separated from non-expired vaccines, and to extend this practice for other medicines to enhance pharmacy practice at the pharmacy in the interest of patient safety.

3.4.5.3 Follow-up audit and corrective and preventive actions

A follow-up audit was performed after 8 weeks. CAPAs (n=8) were implemented to ensure patient safety following educational discussion between the auditor and the pharmacist during the CPRA.

- The point-of-sale system was reviewed to identify if any Hepatitis A and B adult vaccines were dispensed in the last 10 months to ensure that patients have not been dispensed expired vaccines.
- All 4 expired vaccines were disposed of according to the correct licensed waste management procedure.
- To prevent dispensing of expired vaccines and other medicines in the refrigerator, a container to store expired items was placed in the refrigerator, with a label ‘Expired: Do not use’ affixed on the front of the container. The expired medicine area was also labelled.
- The point-of-sale electronic system was updated to include the inputting of expiration dates to help with the identification of expired medicines.
- An expiration date report is being issued monthly and expired medicines from the shelves, drawers or refrigerator are removed accordingly.
- All stock expiration dates are checked manually every 3 months.
- Expiration dates are being checked before dispensing.

- Short-dated medicines are identified by methods of alert, such as collecting them using rubber bands or using a coloured label. The alerts are used on products expiring within the next 3 months.

Concordance was reached between the pharmacist and the auditor, which was confirmed by the follow-up audit to ensure that expired medicines that can threaten patient safety are not dispensed.

3.4.6 Case study 6: Refrigerator temperature below 2°C

During a CPRA, the two refrigerators present at the pharmacy being used to store medicines were showing temperatures below 2°C. The thermometer of the refrigerator containing private pharmacy medicines was showing a temperature of -0.3°C and the thermometer of the refrigerator containing POYC medicines was showing a temperature of - 0.5°C. Temperature records were not being kept updated on a daily basis; the last observed entry was 45 days before the CPRA, implicating that the pharmacist was not monitoring temperature regularly and not restarting the thermometer daily. Refrigerators were observed to contain large quantities of frost. The medicines stored in these refrigerators were insulins, vaccines, hormones, human glucagon and antibodies. All the medicines in the refrigerator were placed in paper bags and sealed using the customised 'Malta Medicines Authority' adhesive tape. The medicines that were exposed to temperature below 2°C are presented in Appendix 3.

3.4.6.1 Implications to patient safety

A table for the identified medicines was compiled from the review of stability data including the identified product trade name and active ingredient/s, visual appearance, storage conditions, allowed excursions, stability implications and sources of information (Appendix 3).

Insulin is extremely sensitive to light and extremes of temperature, hence requiring protection from light and storage between 2°C and 8°C (Cohen et al, 2007). When insulin is exposed to freezing temperatures it loses its potency and biological activity (Wilcox, 2005). As in this case, incorrect storage of insulins is mainly due to accidental freezing. The stability studies for all insulins show a satisfactory physical and chemical stability when stored between 2°C and 8°C. All insulin dossiers document stability at temperatures below 25°C and all results show that insulin levels retained effectiveness for a shorter period compared to storage at 2°C and 8°C. No stability studies for insulins identified in this case were carried out at freezing conditions (below 2°C), hence it cannot be concluded that the insulins in this pharmacy remained stable. Literature shows that insulins should never be frozen or directly exposed to heat or light. When insulin solutions are exposed to freezing, insulin will precipitate after thawing and the precipitate will dissolve once brought back to room temperatures (Pickering et al, 2006; Cuhadar et al, 2013). The insulin will undergo deamidation and rendered unstable. A change in the appearance of insulin results due to aggregation when an insulin suspension is exposed to freezing and it becomes lumpy and granular, rendering it difficult to withdraw the right dose and influencing the onset and duration of action (Hamborsky et al, 2015). The desirable effect from the insulin is likely not reached and negative implications to patient

outcomes may result such as hyperglycaemia, in turn affecting patient outcomes and safety (Hillson, 2015).

Appropriate storage and handling of vaccines is important. Rates of vaccine-preventable diseases have decreased due to appropriate storage and handling of vaccines (Hamborsky et al, 2015). When vaccines are exposed to temperatures outside their recommended storage conditions (2-8°C), decreased potency and reduction in effectiveness and protection can threaten patient safety. In this case, stability studies indicate that Varilrix®, a vaccine that protects against the varicella zoster virus infection[32], shows a reduction in potency if frozen, while Vaxigrip®, a vaccine that protects against seasonal influenza[33] is unstable when exposed to temperatures below 2°C. Although varicella usually presents as an acute infection and is generally self-limiting, it can also be associated with complications, such as secondary bacterial infection, pneumonia and central nervous system manifestations. Secondary bacterial infections of skin lesions with *Staphylococcus* and *Streptococcus* are the most common cause of hospitalisation and may be fatal. Viral or bacterial pneumonia is another complication which may result from contracting the varicella virus. This is especially common in children under 1 year. Central nervous system manifestations range from aseptic meningitis to encephalitis. Although contracting the seasonal influenza virus is not usually accompanied with a serious risk to patient health, in extremes of age and in immunocompromised individuals, influenza may result in serious complications leading to hospitalisations, mainly due to

[32] GlaxoSmithKline. Varilrix vaccine - Summary of Product Characteristics [Online]. UK: eMC; 2017 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/product/1676/smpc

[33] Sanofi Pasteur. Inactivated influenza vaccine (Split virion BP) - Summary of Product Characteristics [Online]. UK: eMC; 2018 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/product/1395/smpc

pneumonia (Hamborsky et al, 2015). Vaccines exposed to extremely low and freezing temperatures, as identified in this pharmacy, can threaten patient safety.

Stability reports for Avonex®, Eporatio®, Glucagen®, Nuvaring®, Ovitrelle® and Prolia® all are similar with regards to excursions in temperature. These medicines were not studied for stability at temperatures below 2°C, except Ovitrelle® which was studied and is stable for 72 hours at temperatures of -20°C. All these medicines showed some degree of stability at temperatures above 8°C, ranging from 7 days to 18 months. The same conclusion, as for insulins and vaccines, can be drawn from the analysis of their stability data, that temperatures below 2°C and freezing temperatures may threaten patient safety by alteration of the safety profile of the medicine and the beneficial therapeutic outcomes.

Using ineffective Avonex®, a recombinant interferon indicated for multiple sclerosis, may result in relapse of the condition and attacks of demyelination.[34] Eporatio® is a recombinant erythropoietin hormone used for symptomatic anaemia. Ineffective Eporatio® may result in untreated anaemia, which may cause a decline in arterial oxygen, negatively affecting organs, such as the heart and the kidneys, with an increased risk of hospitalisation and mortality (Patel et al, 2009; Miller, 2013).[35] Using ineffective Glucagen®, indicated to treat severe hypoglycaemia, may threaten patient safety since

[34] European Medicines Agency. Avonex European Public Assessment Report [Online]. London: European Medicines Agency; 2011 [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/000102/WC500029423.pdf

[35] European Medicines Agency. Eporatio European Public Assessment Report [Online]. London: European Medicines Agency; 2009 [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/001033/WC500043301.pdf

hypoglycaemic reactions will not be resolved, leading to increased risk of cardiovascular and neurological complications (Cryer, 2007; Kalra et al , 2013).[36]

The hormonal contraceptive Nuvaring® will become ineffective when exposed to temperatures below 2°C and may lose contraceptive effectiveness.[37] The hormone choriogondaotropin present in Ovitrelle® is indicated in the treatment of infertility. If an ineffective hormone is administered, ovulation may not be triggered, hence resulting in ineffective treatment.[38] Prolia® contains the monoclonal antibody denusomab and is indicated to treat osteoporosis and bone loss. Denusomab protects the breakdown of bone tissue by reducing the formation and activity of osteoclasts receptor activator of nuclear factor kappa-B ligand. Ineffective Prolia® may predispose the patient to a higher risk of fractures due to uncontrolled osteoclast activity during the 6 months of therapy.[39]

[36] NovoNordisk. GlucaGen Hypokit 1mg - Summary of Product Characteristics [Online]. UK: eMC; 2015 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/product/1289/smpc

[37] Merck Sharp and Dohme Ltd. Nuvaring - Summary of Product Characteristics [Online]. UK: eMC; 2018 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/product/6449

[38] European Medicines Agency. Ovitrelle European Public Assessment Report [Online]. London: European Medicines Agency; 2011 [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/000320/WC500051447.pdf

[39] European Medicines Agency. Prolia European Public Assessment Report [Online]. London: European Medicines Agency; 2015 [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/001120/WC500093527.pdf

3.4.6.2 Educational approach during the audit

During an informal educational discussion between the pharmacist and the auditor during the CPRA, the auditor performed 9 educational interventions:

(1) The auditor explained the implications on patient outcomes and safety if such inappropriately stored medicines reach the patient. This was done for each medicine found.

(2) The auditor stressed the requirement and importance of regular temperature monitoring to ensure appropriate cold chain management. All refrigerated medicines should be stored between 2°C and 8°C, with a desired mean refrigerator storage temperature of 5°C.

(3) The auditor explained actions to be taken if an excursion in temperature is detected. Action should be taken immediately to avoid any implications to patient outcomes and safety. The auditor explained that medicines exposed to temperature excursions should not be dispensed and should be quarantine for disposal. Actions for excursions in temperature include contacting the product Marketing Authorisation Holder, referring to the summary of product characteristics or contacting the MMA for assistance and advice.

(4) The auditor suggested attaching the temperature recording log to the door of the refrigerator to record temperature daily, and to keep these logs filed rather than using a bound register, to decrease the likelihood of forgetting to log temperatures.

(5) The auditor explained that newer technology to avoid temperature excursions is available, such as pharmaceutical grade refrigerators and data loggers. The latter record temperatures automatically.

(6) The auditor recommended that if the pharmacist is too busy with other activities, temperature recording should be assigned to non-pharmacist staff working at the pharmacy, ensuring that an effective system is in place, including developing a SOP for temperature monitoring.

(7) The auditor highlighted that freezing temperatures could have resulted in the presence of frost in the two refrigerators. Defrosting when frost starts to accumulate can prevent temperatures from dropping below 2°C. Servicing the units at least annually will indicate whether the refrigerator is still able to keep stable temperatures between 2°C and 8°C.

(8) The auditor explained the correct way to use thermometers by providing a demonstration. Thermometers should be restarted on a daily basis since the thermometer detects the lowest and highest temperature reached by indicating the maximum and minimum temperature respectively. If the thermometer is not restarted daily and for example the lowest temperature was not detected on day 0, the thermometer will still show that temperature as the minimum until the thermometer is restarted. The thermometer should be restarted daily to detect temperature fluctuations on a daily basis.

(9) Thermometers should be calibrated annually to ensure that temperature readings are accurate.

The auditor and the pharmacist agreed that CAPAs will be implemented to avoid refrigerator temperature fluctuations to enhance pharmacy practice at the pharmacy to improve patient safety.

3.4.6.3 Follow-up audit and corrective and preventive actions

A follow-up audit was performed after 8 weeks. CAPAs (n=11) were implemented by the pharmacy to ensure patient safety following the educational discussion with the auditor during the CPRA:

- A SOP for temperature monitoring was developed and staff were trained.
- The pharmacist assigned the responsibility of daily temperature monitoring to non-pharmacist staff after appropriate training by the pharmacist.
- Temperature records were being recorded daily, including the maximum and minimum readings, and filed in a dedicated file.
- Temperature log was posted on the door of each refrigerator.
- Thermometers are being restarted every day.
- Temperature monitoring is being confirmed by re-checking temperature records daily by the pharmacist.
- The refrigerator is being inspected every day for any accumulation of frost.
- Refrigerators are being defrosted as needed.
- Any medicines exposed to temperature excursions are separated in a container and labelled as 'DO NOT DISPENSE'.
- Plan is for thermometers to be calibrated annually (as requested by the Report of Calibration).
- The pharmacist is considering changing the thermometers to digital data loggers equipped with an alarm system for out-of-range temperature readings and changing the refrigerators to pharmaceutical grade refrigerators.

Concordance was reached between the pharmacist and the auditor which was confirmed by the follow-up audit to ensure temperatures are within the acceptable range to safeguard patient health and safety.

3.4.7 Case study 7: Inequity towards patients

During a CPRA, a deficiency related to inequity of treatment between private and government-sponsored (POYC) patients was observed. A patient presented to the pharmacy to collect the POYC medicines. The pharmacist was dispensing a private prescription for an antibiotic with counselling when this patient entered the pharmacy. The pharmacist instructed a non-pharmacist to provide the prepared POYC medicines to the patient. The non-pharmacist gave the pack with the medicines to the pharmacist and the pharmacist dispensed the medicines to the patient without double-checking or providing advice. The auditor identified this deficiency related to patient safety and brought it to the attention of the pharmacist. During an educational discussion during the CPRA, the pharmacist stated that the pharmacy has over 950 registered POYC patients and that the POYC system is time-consuming and problematic. The pharmacist stated that giving priority to private patients over POYC patients was an unintentional discrimination and acknowledged the deficiency. The pharmacist explained that this unintentional discrimination may have resulted due to patients presenting at the pharmacy requesting an instantaneous professional service and not being willing to wait.

3.4.7.1 Implications to patient safety

Equal access to healthcare is considered a right for patients. An important issue of health equity is equal access to health services to those in need (Hendryx et al, 2002; Yavari et al, 2015). In this case, the POYC service was not being given equal importance as private pharmacy services. This could have had many negative implications towards patient care and safety. POYC patients are usually taking more than one medicine and are at risk of polypharmacy issues. The packaging of POYC medicines is constantly changing, hence patients, especially illiterate patients, are more prone to confusion and medication errors. The pharmacist cannot assume that the patient knows the correct use of the medicines and the correctness of the dispensed medicines (Embrey, 2012). Dispensing POYC medicines without checking will not detect medication errors, such as omission or addition of a drug, and incorrect dose/dosage regimen, non-compliance, and risk for drug interactions.

3.4.7.2 Educational approach during the audit

During an informal educational discussion between the auditor and the pharmacist during the CPRA, the auditor carried out 6 educational interventions:

(1) The auditor stressed the importance that the pharmacist should provide equal and effective healthcare to all patients presenting at the pharmacy, irrespective of whether the patients are paying for the service or not, as in this case of POYC patients.
(2) The auditor highlighted the need to safeguard patient health through effective communication with all patients, including POYC patients.
(3) The auditor reminded the pharmacist that as a healthcare professional in the community setting the pharmacist has the last contact with the patient before consumption of the medicine.

(4) The pharmacist was made aware about the negative implications to patient safety related to dispensing POYC medicines without re-checking, such as polypharmacy issues and confusion leading to medication error/s due to for example the constant changes in the outer packaging of POYC medicines.

(5) The need to reduce waiting time when faced with many patients requesting services was acknowledged during the educational discussion, however, the pharmacist should be aware that it is the responsibility of the pharmacist to offer excellent services to both private and POYC patients to ensure patient safety. An appropriate dispensing service is more important than speed of delivery.

(6) The auditor acknowledged that the POYC system may be time-consuming and problematic, however explained that it should not be considered as an extra load to pharmacy services.

The auditor and the pharmacist agreed that CAPAs will be implemented to provide equal professional pharmacy services, irrespective of private or government-sponsored patients to enhance pharmacy practice at the pharmacy in the interest of patient safety.

3.4.7.3 Follow-up audit and corrective and preventive actions

A follow-up audit was performed after 8 weeks. CAPAs (n=4) were implemented to ensure patient safety following the educational discussion between the auditor and the pharmacist:

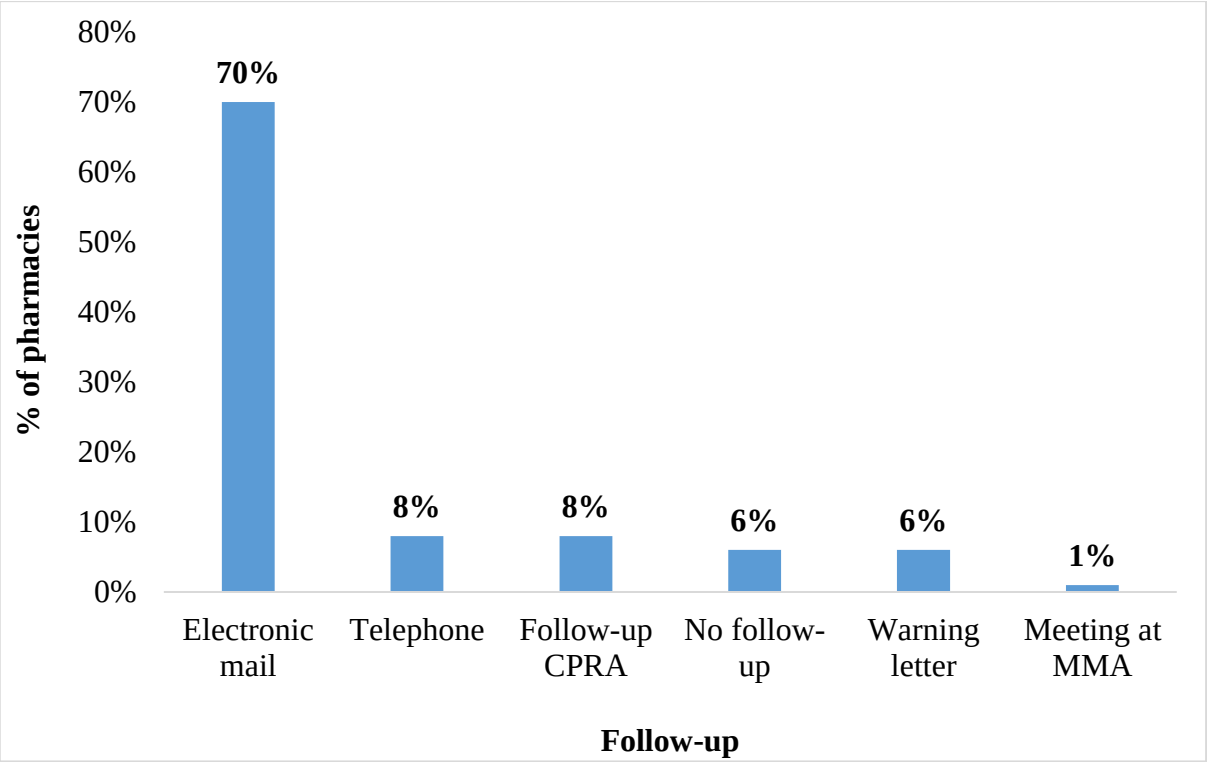
- A pharmacy technician was employed at the pharmacy to work out POYC medicines to manage better with the 950 registered patients, however the pharmacist stated that dispensing will always be carried out by the pharmacist on duty.

- Prioritisation is being practiced at the pharmacy, such as point-of-sale activities and cosmetic-related queries are being dealt with by non-pharmacist staff, while the pharmacist is focusing and prioritising activities related to medical ailments irrespective of private and government-sponsored patients.
- Medicine-use reviews are being provided free-of-charge to all patients presenting with problems with the medicines.
- To ensure equity with all POYC patients, a new POYC system was implemented in the pharmacy, where a patient prescribed a small number of POYC medicines (≤ 3 medicines) are served at that time, while longer orders (≥ 4 medicines) are served within 1 day.

Concordance was reached between the pharmacist and the auditor, which was confirmed by the follow-up audit, to ensure equal attention is given to all patients to safeguard equity of patient care and patient safety.

3.5 Follow-up of CPRAs

Follow-up audits were performed in 5 different ways in the community pharmacies where deficiencies related to regulation or to patient safety were identified. Seven CPRAs were not followed-up since no deficiencies were identified during the CPRA, while the other CPRAs with identified deficiencies were followed-up in one or more than one way (Figure 3.5).



CPRA: Community Pharmacy Regulatory Audit; MMA: Malta Medicines Authority

Figure 3.6: Representation of follow-up of CPRAs in 2017 (N=111)

3.6 Dissemination of results

An abstract titled *'Reaching Concordance in Community Pharmacy Regulatory Audits'* was accepted for poster presentation at the 78th FIP World Congress of Pharmacy and Pharmaceutical Sciences 2018, to be held in Glasgow, Scotland, from 2-6 September 2018 (Appendix 4).

An abstract titled *'Patient-Centred Regulatory Audits in Community Pharmacy'* was accepted for poster presentation at the 2018 American College of Clinical Pharmacy Global Conference on Clinical Pharmacy, to be held in Seattle, United States of America, from 20-23 October 2018 (Appendix 4).

Chapter Four

Discussion

4.1 Evolving community pharmacy regulatory audits to improve patient safety

The pharmacy profession has evolved towards patient-centred practice and pharmacy practice has evolved from compliance and adherence to concordance. In this research, the way in which the regulation of community pharmacy could adopt the same concepts and evolve towards patient-centred regulatory audits was studied and patient-centred community pharmacy regulatory audits (CPRAs) were developed and implemented. The research explored whether concordance between the auditor and the pharmacist in CPRAs can be reached through employing an innovative educational approach, and assessed if concordance in CPRAs can lead to optimised patient-centred practice. Through this research, CPRAs evolved from adopting a predominantly policing approach towards adopting an innovative educational approach reaching concordance in the interest of patient safety and care outcomes.

The retrospective analysis of CPRA reports extracted features that could lead to the identification of patient-related deficiencies in community pharmacy practice. The retrospective analysis indicated that CPRAs were only assessing compliance to regulatory and legislative requirements and were not assessing pharmaceutical care provision by the community pharmacist. The primary focus of CPRAs before this research was on product quality and the characteristics of the pharmacy and CPRAs were not assessing patient safety through the provision of appropriate pharmaceutical care by pharmacists in daily practice. The findings from the retrospective analysis indicated non-compliance to regulatory and legislative requirements, such as inadequate daily monitoring and recording of ambient and refrigerator temperatures, inadequate annual calibration of thermometers and lack of standard operating procedures implemented in community

pharmacies. These identified features are considered as potentially threatening to patient safety.

The policing approach adopted in CPRAs before this research was confirmed through the way follow-up communication after a CPRA was being performed. A policing approach in CPRAs adopted forceful enforcement to obtain compliance to regulatory and legislative requirements through the issue of warning letters and through instructions with stringent timelines, such as to present updated registers to the Malta Medicines Authority (MMA) by the end of the month after the CPRA. In CPRAs with a policing approach, the pharmacist had to comply to strict instructions and there was no room for discussion and education on the deficiencies identified and on the implications to patient safety. Through punitive enforcement, the attributes and competences of the community pharmacist in the provision of pharmaceutical care were not assessed and this type of CPRA did not motivate the pharmacist towards improved pharmacy practice. The policing-approach in CPRAs was unidirectional, with data collection carried out only to satisfy regulation and legislation requirements.

The informal one-to-one interviews with the community pharmacists identified limitations of and improvements to the CPRA to enhance patient safety and community pharmacy practice. The interviews revealed a gap in communication between the regulatory body (MMA) and the community pharmacists. The pharmacists stated that the policing approach in CPRAs was resulting in pharmacist demotivation, stress and dissatisfaction, and that the pharmacists wanted to see a change in the way CPRAs are performed by incorporating a more patient-centred approach. Negative perceptions of the

CPRA risk inadequate provision of pharmaceutical care by pharmacists, which in turn can negatively impact patient safety (Rapport et al, 2010). Results of the retrospective analysis and the interviews with the community pharmacists were important to implement reform in the approach adopted in CPRAs.

An innovative, educational, patient-centred approach was adopted in CPRAs in this research to reach concordance between the regulator and the community pharmacist, distinct to forceful compliance. The CPRA was implemented in two parts; documentation and observation, adopting an educational approach throughout the CPRA process. An educational approach was implemented to evolve the CPRA from a predominantly 'compliance/conformance' CPRA towards becoming a 'performance' CPRA. Implementing 'performance' CPRAs led to the identification of deficiencies in pharmacy practice related to patient safety.

The CPRA tool was updated according to results from the retrospective analysis and the interviews with the community pharmacists and was used to assess compliance to regulation and legislation during documentation. The educational approach was maintained during documentation by mapping regulation and legislation to each requirement in the checklist of the CPRA tool to facilitate explanation and discussion of each requirement by the auditor during the CPRA. An innovative observation approach by the auditor was successfully integrated in CPRAs through this research to identify patient-related deficiencies which could threaten patient safety. Introduction of this innovative observation in CPRAs was feasible since, as a pharmacist, the auditor (researcher) has the competences to identify these deficiencies in pharmacy practice

(Rapport et al, 2010). Questions, such as 'Do you dispense Prescription-Only-Medicines (POMs) without a prescription?' or 'Do you provide effective pharmaceutical care?', cannot be asked by an auditor during a CPRA, since the pharmacist is likely to respond as 'No' to dispensing POMs without a prescription' and as 'Yes' to the provision of effective pharmaceutical care, hence an accurate reflection of what is actually being performed may not be obtained. Direct observation during a CPRA facilitates the accurate identification of patient-related deficiencies in pharmacy practice.

The innovative observation approach adopted in CPRAs through this research was supported by concepts of education and Berwick's 'Theory of Continuous Improvement' (Knowles, 1985; Berwick, 1989; Knowles et al, 2015; Flores et al, 2016). An educational approach in CPRAs is bidirectional facilitates cooperation and seeks continuous improvement in pharmacy practice (Berwick, 1989, Wiederholt et al, 2002). In turn, an educational approach may improve pharmacist performance towards patient-centred care (Shapiro et al, 1997; Wiederholt et al, 2002). The identified deficiencies were discussed with the pharmacist during the CPRA and concordance on corrective and preventive actions (CAPAs) was reached between the auditor and the pharmacist. Follow-up CPRAs were performed to assess implementation of CAPAs for the identified deficiencies in the interest of patient safety. The concept of concordance (Marinker et al, 1997; Foster et al, 1998; Britten, 2007) is widely used in the clinical scenario (Watson, 2009; Snowden et al, 2013) and was adopted in CPRAs through this research. The observed deficiencies related to patient safety were evaluated as seven case studies. The median time taken to carry out a CPRA using the updated audit tool, observation of patient-centred practice and educational discussions (70 minutes) and a follow-up CPRA (30 minutes) was deemed practical and feasible, allowing auditors time to perform other duties at the MMA.

The informal educational discussions between the auditor and the pharmacist during the CPRA were the basis of the educational approach. According to Coles (1989), "people learn best when they are helped to define their own problems, acknowledge and accept their strengths and weaknesses, decide on a course of action and evaluate the consequences of their decisions". This statement can be translated to this research since the educational discussions during the CPRA helped to identify deficiencies and the implications to patient safety and helped to acknowledge the need for implementing changes as CAPAs through concordance to improve patient safety, care outcomes and pharmacist motivation.

Figure 4.1 shows how a deficiency related to patient safety identified during a CPRA relates to the patient. A deficiency is identified by documentation using the audit tool and by direct observation. Through an informal educational discussion during the CPRA, the auditor discusses implications to patient safety of the identified deficiency with the pharmacist. The deficiency may relate directly to the patient, as observed in the case studies evaluated, namely 'a dispensing error of methotrexate 2.5mg instead of methyldopa 250mg', 'a near-miss medication error', 'dispensing a POM without a prescription', 'filling of prescriptions by non-pharmacist staff' and 'inequity towards patients', or may affect the quality of the product, in turn threatening patient safety, such as 'expired vaccines' and 'refrigerator temperature below 2°C' (section 3.4).

Educational interventions by the auditor, including recommending CAPAs to improve patient safety, are performed and concordance with the pharmacist on CAPAs is achieved. Implementation of CAPAs is checked by the auditor during a follow-up CPRA. Implementation of CAPAs will have a positive outcome on the patient due to improved patient safety and care outcomes. An educational approach throughout the CPRA and cooperation between the auditor and the pharmacist encourages concordance.

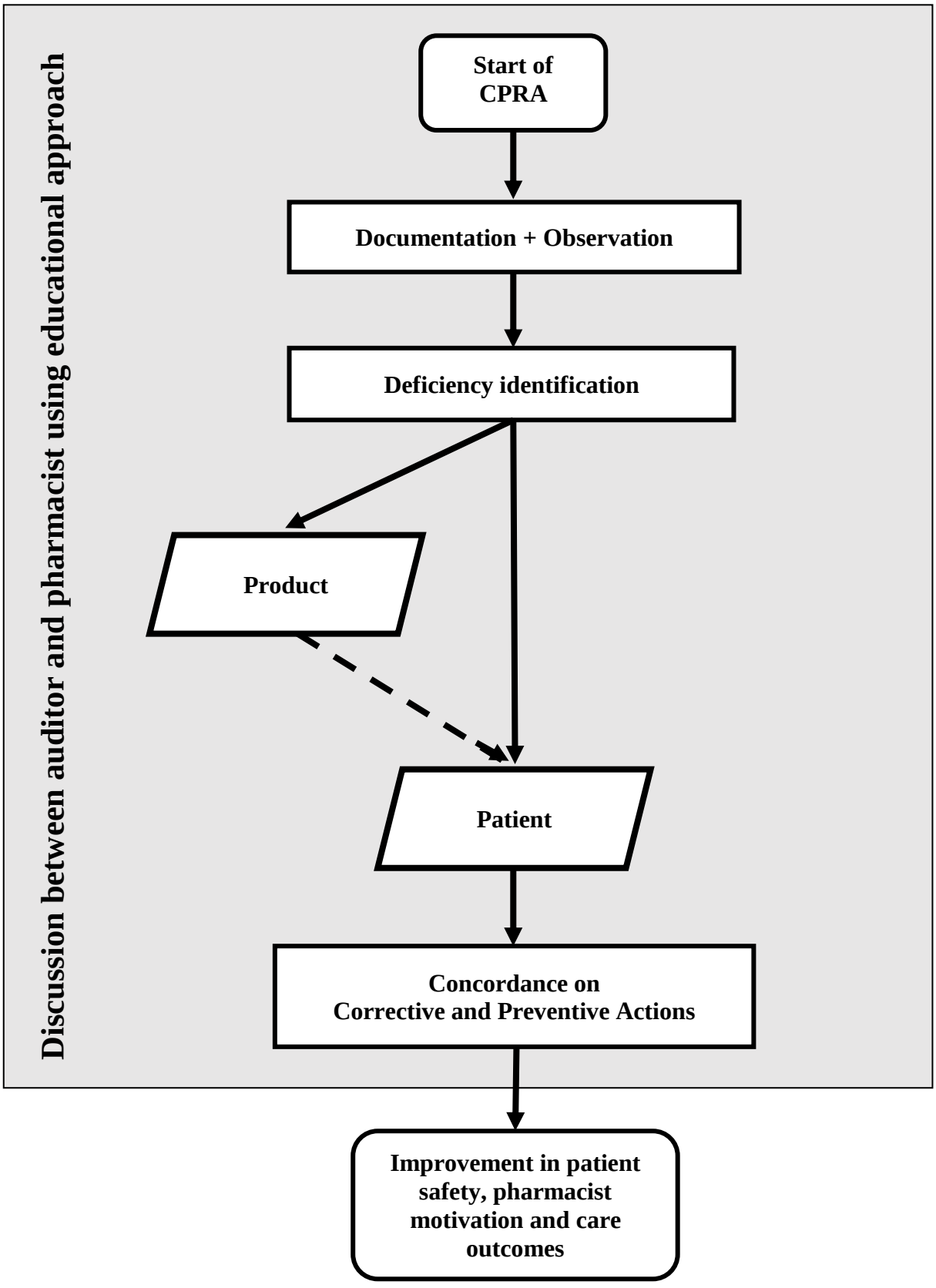


Figure 4.1: Flow diagram relating the identified deficiencies to patient safety in CPRAs

The identified outcomes from the case studies evaluated and from the educational discussions between the auditor and the pharmacists, as well as the CAPAs implemented to address the identified deficiencies related to patient safety in this research, can be implemented as preventive actions to enhance patient safety and care outcomes in all community pharmacies in Malta and Gozo.

Examples of preventive actions implemented in the case studies evaluated that may be applied in other pharmacies are; ensuring that dispensing is always performed by or under the direct supervision of a pharmacist; implementing precautions to avoid dispensing errors especially for cytotoxic and high-alert medicines, such as labelling of shelves and implementing methods of alert for 'sound-alike', 'look-alike' and 'written-alike' medicines, and on short-dated medicines to ensure double-checking before dispensing; performing routine stock rotation to prevent dispensing of expired medicines, and implementing electronic systems. SOPs for community pharmacy practice should be implemented, such as for referral of patients to the pharmacist for ailments involving medicine dispensing and for temperature monitoring. 'Dispensing errors' and 'near-miss medication errors' records can be introduced and checked during the CPRA to continuously improve pharmacy practice in favour of patient safety. Recording errors may facilitate identification of any patterns to prevent recurrences. Employing improved methods of communication and provision of advice to patients, such as increasing awareness of the Pregnancy Prevention Programme and the availability of acknowledgment forms at the pharmacy for topical and oral retinoid therapy may prevent patient harm and safeguard the pharmacy profession.

4.2 Philosophical theories and concepts of quality of care and education: Application to community pharmacy regulatory audits

Berwick's 'Theory of the Bad Apple' represents the policing approach in CPRAs adopting forceful enforcement. This theory can be applied to compliance/conformance-CPRAs, which are carried out to identify findings of non-compliance (Russell, 2013). Non-compliance findings reflect the 'bad apples' in Berwick's theory and must be corrected or 'removed' through issue of warning letters and compliance and adherence to strict timelines.

The assumptions of andragogy (Knowles, 1989; Holyoke et al, 2009; Knowles et al, 2015; Flores et al, 2016) were adopted in the CPRAs implemented. The assumption of pharmacists as 'self-directed learners' was implemented by encouraging cooperation and concordance between the auditor and the pharmacist through an educational discussion during the CPRA, as opposed to enforcing compliance. The auditor motivated the pharmacist towards willingness to implement CAPAs to enhance patient safety, as stated in the sixth andragogy assumption 'motivated to learn'. The community pharmacists were viewed as 'experienced' and 'ready-to-learn' through reaching concordance to CAPAs, fulfilling the second and third assumption of the concept of andragogy. The pharmacist was 'oriented towards learning' through engaging in informal educational discussions with the auditor during the CPRA to address the identified deficiencies related to patient safety by implementing CAPAs. For each identified deficiency the auditor explained the implications to patient safety, satisfying the assumption of the 'need to know the reason' for the requirement of CAPAs.

The educational approach implemented in the CPRAs relates to Berwick's 'Theory of Continuous Improvement' (Berwick, 1989). The auditor can be likened to the second foreman referred to in 'The Theory of Continuous Improvement' who identified opportunities for improvement (Berwick, 1989). The auditor identified deficiencies related to patient safety during the CPRA and the educational approach adopted promoted continuous improvement in pharmacy practice in favour of patient care outcomes.

The patient-centred CPRA can be metaphorically compared to a flight. Metaphorical thinking helps to understand the approaches and outcomes implemented in this research to a recognisable situation (Sanchez-Ruiz et al, 2013; Wood, 2015).

The aeroplane represents the regulatory body, in this case the MMA, the pilot and the co-pilot represent the pharmacist and the auditor respectively who must work as a team, and the passengers represent the patients. The flight holistically denotes the whole CPRA process, which is divided into three stages namely; take off, cruising and landing. The take off and the landing, being the most difficult and crucial stages of the flight, involve a direct interaction between the pilot (pharmacist) and the co-pilot (auditor). During the cruising stage, the co-pilot observes the general correct operation of the flight, identifying any measures which may be necessary during moments of turbulence, representing the deficiencies.

From the flight process, which represents the CPRA, one may deduce certain elements which hold key for a successful flight. Firstly, the pilot (pharmacist) and the co-pilot (auditor) must work as a team, hence an educational approach from the moment that the auditor steps into the pharmacy and initiates the CPRA (take off) is crucial. Through an educational approach, the community pharmacist feels a positive sense of belonging from the start, where the pharmacist is the leader (pilot) and the auditor is the partner (co-pilot) in achieving a successful outcome which benefits the patients (passengers).

During the cruising phase of the flight, interaction between the co-pilot (auditor) and the pilot (pharmacist) takes the back seat, while observation by the co-pilot is given priority. The co-pilot only intervenes in moments of turbulence (deficiencies) which require interaction. Once again, in such moments of turbulence, the educational aspect must be maintained, so that the pilot (pharmacist) feels comfortable and is always willing to employ the co-pilot's (auditor's) advice, in turn safeguarding the passengers' (patients') safety. As the flight approaches landing, the direct interaction takes over again, as the pilot (pharmacist) and co-pilot (auditor) reach consensus on safe arrival at the desired destination. This symbolises the concordance aspect which lies at the core of this research towards implementation of a patient-centred CPRA.

It is futile having the best equipped and most attractive aeroplane (MMA) if the pilot (pharmacist) and the co-pilot (auditor) are unwilling to work as a team, hence endangering passenger (patient) safety. This metaphor portrays the importance of this research towards developing patient-centred CPRAs, guided by a continuous educational approach during the CPRA. Referring back to the aeroplane metaphor, a smooth flight (CPRA) with

minimal turbulence (deficiencies), ensures passenger (patient) safety, while motivating the pilot (pharmacist) and the co-pilot (auditor) to strengthen their co-operation. Conversely, a bad take-off or landing, combined with unmitigated turbulence (deficiencies), endangers passenger (patient) safety and contributes towards higher tensions, which deteriorate the working relationship between the pilot (pharmacist) and the co-pilot (auditor). Further to the metaphorical comparison, cabin crew have an important role in the flight process. Cabin crew may represent pharmacy technicians and pharmacy assistants who perform important activities in a well-functioning community pharmacy with a patient-centred approach.

Providing the community pharmacist with a sense of belonging through discussion and education was crucial towards successful implementation of patient-centred CPRAs. As portrayed in the metaphorical comparison, the community pharmacists were engaged in CPRAs as ‘leaders’, ‘decision-makers’, ‘life-long learners’ and ‘care givers’. It is only through such direct engagement and interaction between the regulator and the community pharmacist that CPRAs could have evolved towards reaching concordance on corrective and preventive actions in the interest of patient safety.

4.3 Strengths and limitations of the research

All pharmacies who had a renewal or spot-check CPRA performed in 2017 were included and selection bias was avoided since the pharmacies were audited according to a pre-set audit plan and were not selected by the researcher through convenience sampling. Pharmacists were not selected according to age, gender or years of experience, reducing bias in the results. Since a CPRA is unannounced, the auditor was not aware of the details of the pharmacist who will be at the pharmacy at the time of the CPRA. This was important to avoid bias in the results since the pharmacies and the pharmacists were not selected by the researcher by convenience sampling.

Both managing pharmacists and locum pharmacists were encountered during the CPRAs, allowing extension of the educational patient-centred approach also to locum pharmacists. However a limitation was that in instances when the managing pharmacist, who is responsible for ensuring that the pharmacy is in accordance to regulatory and legal requirements and who takes the final decision on implementation of CAPAs, was not present (27% of the CPRAs). These managing pharmacists were not exposed to the innovative educational approach implemented in the CPRA, hence may still have retained the perception of a CPRA adopting a policing and forceful enforcement approach.

The CPRA tool was validated by two community pharmacists selected by convenience sampling. Validation of the tool by a larger number of community pharmacists selected by random sampling may have led to more discussion and amendments to the tool. The focus group set up for the methotrexate dispensing error consisted of three community pharmacists who were also selected by convenience sampling. Inclusion of a larger

number of community pharmacists and selected by random sampling may have led to identification of further root causes for errors and recommendations.

Although an educational approach was implemented in the CPRAs to reach concordance, punitive enforcement by means of a warning letter was still issued for pharmacies where deficiencies related to temperature monitoring and recording were identified (7 pharmacies), since this action is stipulated in the quality management system (QMS) of the MMA. Further to this research, it is proposed that that the QMS should be updated to revise methods of forceful enforcement in instances when concordance to implement CAPAs is reached between the auditor and the pharmacist.

4.4 Recommendations

It is recommended that updates to the CPRA tool should be continuous according to discussions with and feedback from the community pharmacists during future CPRAs.

Findings obtained in the subsequent CPRA carried out in the same pharmacies audited in this research can be compared to assess improvement in compliance to regulatory and legislative requirements (documentation) as a result of implementation of an educational approach in CPRAs.

Further studies to quantitatively measure the improvement in patient safety, patient care outcomes and pharmacist motivation as a result of implementation of patient-centred CPRAs could be undertaken.

The possibility of introducing goal-oriented initiatives, such as issue of a 'Good Pharmacy Practice' certificate following a CPRA and not simply renewal of the pharmacy license, may be explored to enhance pharmacist motivation towards CPRAs. Such an initiative was adopted in Uganda in 2014, where a GPP certificate is issued to pharmacists adhering to regulatory requirements (Trap et al, 2016). In the context of the patient-centred CPRAs implemented in this research, it is proposed to explore awarding of these certificates according to pharmacist performance towards patient care, which can be assessed by the auditors according to agreed criteria for patient-centred care, such as communication skills with patients; medication control, including medication errors, dispensing without prescription; drug therapy monitoring; advice provision; accessibility to patients and equity of treatment. This initiative can be compared to the 'Quality Assured' scheme implemented by the Malta Tourism Authority in 2008 with the aim to recognise businesses offering a high level of quality, consistency and professionalism.[40] The same principle can be applied for pharmacies and pharmacists according to performance of the criteria for patient-centred care.

The patient-centred approach adopted in CPRAs should be disseminated to all pharmacists, particularly pharmacists who were not exposed to the reform in the CPRAs through this research, by organising educational seminars. These seminars will serve as an outreach by the auditors to explain to the pharmacists what a patient-centred CPRA entails and to discuss examples of preventive actions identified in the case studies evaluated that can be implemented to improve patient safety and care outcomes in community pharmacy practice.

[40] Malta Tourism Authority. Quality assured seal [Online]. Mta.com.mt. 2018 [cited 2018 May 30]. Available from: URL: http://www.mta.com.mt/quality-seal

The possibility of analysis of deficiencies related to patient safety by the pharmacists identified during their daily practice may be explored as a requirement of the CPRA for good pharmacy practice and to enhance the concept of a patient-centred CPRA, for example by evaluating 10 case studies yearly.

The patient-centred educational approach adopted for CPRAs in this research should be extended to audits of hospital pharmacies to improve patient safety and care outcomes.

Updating of the MMA QMS is proposed to revise methods of forceful enforcement in instances when concordance to implement CAPAs is reached between the auditor and the pharmacist.

Continuation of these patient-centred CPRAs contributes to keep improving patient safety, care outcomes and pharmacist motivation in community pharmacy practice. The MMA should strive to continue to equip its auditors with relevant competences and expertise through training to ensure sustained implementation of this educational approach in CPRAs to identify patient-related deficiencies and to reach concordance in favour of patient safety.

Areas for improvement identified through the interviews with the community pharmacists and from the methotrexate focus group discussion which warrant further study are the implementation of national strategies to reduce dispensing errors in community pharmacy

practice, discussion towards the legal changes required to empower pharmacists to prescribe, performance of medicine use reviews for patients with chronic conditions, and improving the Pharmacy-Of-Your-Choice system in favour of patient safety, such as through introduction of drug-drug interaction detection software.

4.5 Conclusions

This research evolved the CPRA from adopting a predominantly policing approach with forceful enforcement towards a patient-centred CPRA adopting an innovative educational approach, where concordance between the auditor and the pharmacist was reached to improve patient safety and care outcomes.

Using punitive enforcement as a motivator many times induces fear and has been identified as a barrier for quality improvement. Implementation of an educational approach in CPRAs improved communication and cooperation between the regulator and the community pharmacist, which led to increased pharmacist motivation to reach concordance on the implementation of patient-centred improvements in community pharmacy practice. CPRAs incorporating educational discussions positively influenced the relationship between the regulator and the pharmacist to reach concordance on corrective and preventive actions to be implemented to improve patient safety and care outcomes.

The researcher reflected that the introduction of the philosophical concept of pharmaceutical care, conjoined with concepts and theories of education and quality in care, to develop patient-centred CPRAs was crucial in identifying the missing gap between the community pharmacist and the regulator. Such an in-depth analysis to address the 'philosophical deficit' in the CPRA process enabled the researcher to develop and implement a practical and innovative proposal which effectively moves away from a regimental form of regulation towards an approach that benefits pharmacy patient-centred practice and makes the work activities of both the community pharmacist and regulators alike very satisfying, albeit challenging.

References

AlGhurair SA, Simpson SH, Guirguis LM. What elements of the patient-pharmacist relationship are associated with patient satisfaction? Patient Preference and Adherence. 2012;6:663–676.

Al-Shaqha W, Zairi M. Pharmaceutical care management: A modern approach to providing seamless and integrated health care. International Journal of Health Care Quality Assurance. 2001;14(7):282-301.

Arnet I, Bernhardt V, Hersberger K. Methotrexate intoxication: The pharmaceutical care process reveals a critical error. Journal of Clinical Pharmacy and Therapeutics. 2011;37(2):242-244.

Awaisu A, Alsalimy N. Pharmacists' involvement in and attitudes toward pharmacy practice research: A systematic review of the literature. Research in Social and Administrative Pharmacy. 2015;11(6):725-748.

Azzopardi LM. Validation instruments for community pharmacy: Pharmaceutical care for the third millennium. 1st ed. New York: Pharmaceutical Products Press; 2000.

Baines D. Pharmaceutical care: The blueprint for modern pharmacy. Prescriber. 2014;25:14-16.

Bates I, John C, Bruno A, Fu P, Aliabadi S. An analysis of the global pharmacy workforce capacity. Human Resources for Health. 2016;14(61):7 pages.

Bell J, Airaksinen M, Lyles A, Chen T, Aslani P. Concordance is not synonymous with compliance or adherence. British Journal of Clinical Pharmacology. 2007;64(5):710-711.

Berwick D. Continuous improvement as an ideal in health care. New England Journal of Medicine. 1989;320(1):53-56.

Bissonnette J. Adherence: A concept analysis. Journal of Advanced Nursing. 2008;63(6):634-643.

British National Formulary Joint Formulary Committee. British National Formulary 74. London: Pharmaceutical Press; 2017.

Britten N. Concordance in medical consultations: A critical review. Journal of Advanced Nursing. 2007;57(5):562-568.

Bugnon O, Hugentobler-Hampai D, Berger J, Schneider MP. New roles of community pharmacists in modern health care systems: A challenge for pharmacy educators and research. Chimia Journal. 2012;66(5):304-307.

Buttigieg F. Community pharmacy quality programmes [project]. Msida (Malta): Department of Pharmacy University of Malta; 2006.

Capen R, Christopher D, Forenzo P, Ireland C, Liu O, Lyapustina S, O'Neill J, et al. On the shelf life of pharmaceutical products. American Association of Pharmaceutical Scientists. 2012;13(3):911-918.

Chakrabarti S. What's in a name? Compliance, adherence and concordance in chronic psychiatric disorders. World Journal of Psychiatry. 2014;4(2):30-36.

Chua SS, Tea MH, Rahman MHA. An observational study of drug administration errors in a Malaysian hospital (study of drug administration errors). Journal of Clinical Pharmacy and Therapeutics. 2009;34:215-223.

Cohen V, Jellinek S, Teperikidis L, Berkovits E, Goldman W. Room-temperature storage of medications labeled for refrigeration. American Journal of Health-System Pharmacy. 2007;64(16):1711-1715.

Coles C. Self-assessment and medical audit: An educational approach. British Medical Journal. 1989;299(6703):807-808.

Coley NG. Medical chemists and the origins of clinical chemistry in Britain (circa 1750-1850). Clinical Chemistry. 2004;50(5):961.

Costa F, Scullin C, Al-Taani G, Hawwa A, Anderson C, Bezverhni Z. Provision of pharmaceutical care by community pharmacists across Europe: Is it developing and spreading? Journal of Evaluation in Clinical Practice. 2017;23(6):1336-1347.

Cousins D, Kijlstra N, Walser S. Pharmaceutical care: Policies and practices for a safer, more responsible and cost-effective health system. Strasbourg: European Directorate for the Quality of Medicines and HealthCare; 2012.

Crijins H, Straus S, Gispen de Wied C, De Jong van den Berg L. Compliance with pregnancy prevention programs of isotretinoin in Europe: A systematic review. British Journal of Dermatology. 2011;164:238-244.

Crowe S, Cresswell K, Robertson A, Huby G, Avery A, Sheikh A. The case study approach. BioMed Central Medical Research Methodology. 2011;11:100.

Crowley S, Hawhee D. Ancient rhetorics for contemporary students. Massachusetts: Allyn and Bacon; 1999. p. 1-19.

Cryer PE. Hypoglycemia, functional brain failure, and brain death. The Journal of Clinical Investigation. 2007;117(4):868-870.

Cuhadar S, Koseoglu M, Atay A, Dirican A. The effect of storage time and freeze-thaw cycles on the stability of serum samples. Medical Biochemistry and Laboratory Medicine Journal. 2013;23(1):70-77.

Dahiya S, Dahiya R, Lodhi NK, Shrivastava SK, Soni L. Patient-oriented pharmacy education and redefining role of pharmacist: A challenge to educationists. Bulletin of Pharmaceutical Research. 2012;2(3):154-158.

De las Cuevas C. Towards a clarification of terminology in medicine taking behaviour: Compliance, adherence and concordance are related although different terms with different uses. Current Clinical Pharmacology. 2011;6(2):74-77.

Duffull S, Wright D, Marra C, Anakin M. A philosophical framework for pharmacy in the 21st century guided by ethical principles. Research in Social and Administrative Pharmacy. 2018;14(3):309-316.

Embrey M. Managing access to medicines and health technologies. Arlington: Management Science for Health; 2012.

Emmerton L, Becket G, Gillbanks L. The application of electronic work sampling technology in New Zealend community pharmacy. Journal of Social and Administrative Pharmacy. 1998;15:191-200.

Fallah A, Deep M, Smallwood D, Hughes P. Life threatening rhabdomyolysis following the interaction of two commonly prescribed medications. Australasian Medical Journal. 2013;6(3):112-114.

Fang Y, Yan K. Politics and competition between professions. Social and administrative aspects of pharmacy in low and middle income countries. 2018;(20):329-341.

Flores K, Kirstein K, Schieber C, Olswang S. Supporting the success of adult and online students. 5th ed. Seattle: City Universal of Seattle; 2016. p. 73-84.

Flynn H. Development of a self-evaluation validation process for community pharmacy [Mpharm dissertation]. Msida (Malta): Department of Pharmacy University of Malta; 2017.

Foster P, Hudson S. From compliance to concordance: A challenge for contraceptive prescribers. Health Care Analysis. 1998;6(2):123-130.

Hagen M, Park S. We knew it all along! Using cognitive science to explain how andragogy works. European Journal of Training and Development. 2016;40(3):171-190.

Hall NJ, Donovan G, Wilkes S. A qualitative synthesis of pharmacy, other health professional and lay perspectives on the role of the community pharmacy in facilitating care for people with long-term conditions. Research in Social and Administrative Pharmacy. 2018;1(2):15 pages.

Hamborsky J, Kroger A, Wolfe C. Epidemiology and prevention of vaccine-preventable diseases. 13th ed. Washington DC: Public Health Foundation; 2015.

Haw C, Stubbs J, Dickens G. An observational study of medication administration errors in old-age psychiatric inpatients. International Journal for Quality in Healthcare. 2007;19(4):210-216.

Hendryx M, Ahern M, Lovrich N, McCurdy A. Access to health care and community social capital. Health Services Research. 2002;37(1):85-101.

Hepler CD, Strand LM. Opportunities and responsibilities in pharmaceutical care. American Journal of Hospital Pharmacy. 1990;47:533-543.

Hepler CD. Clinical pharmacy, pharmaceutical care, and the quality of drug therapy. Pharmacotherapy. 2004;24(11):1491-1498.

Hillson R. Temperature and blood glucose management. Practical Diabetes. 2015;32(7):231-235.

Holloway KA. Combating inappropriate use of medicines. Expert Review of Clinical Pharmacology. 2011;4(3):335-348.

Holyoke L, Larson E. Engaging the adult learner generational mix. Journal of Adult Education. 2009;38(1):12-21.

Horne R, Weinman J, Barber N, Elliott R, Morgan M, Cribb A, et al. Concordance, adherence and compliance in medicine taking. London: National Coordinating Centre for NHS Service Delivery and Organisation; 2005.

Howard S, McCormick J, Pui C, Buddington R, Harvey R. Preventing and managing toxicities of high-dose methotrexate. The Oncologist. 2016;21(12):1471-1482.

Kalra S, Mukherjee JJ, Venkataraman S, Bantwal G, Shaikh S, Saboo B, et al. Hypoglycemia: The neglected complication. Indian Journal of Endocrinology and Metabolism. 2013;17(15):819-834.

Knowles M, Holton E, Swanson R. The adult learner. 8th ed. New York: Routledge; 2015.

Knowles M. Applications in continuing education for the health professions: Chapter five of andragogy in action. Möbius: A Journal for Continuing Education Professionals in Health Sciences. 1985;5(2):80-100.

Lee A, Maddix D. Rhabdomyolysis secondary to a drug interaction between simvastatin and clarithromycin. Annals of Pharmacotherapy. 2001;35(1):26-31.

Li D, Kim R, McArthur E, Fleet J, Bailey D, Juurlink D, et al. Risk of adverse events among older adults following co-prescription of clarithromycin and statins not metabolized by cytochrome P450 3A4. Canadian Medical Association Journal. 2014;187(3):174-180.

Malerba F, Orsenigo L. The evolution of the pharmaceutical industry. Business History. 2015;57(5):664-687.

Marinker M, Royal Pharmaceutical Society of Great Britain. From compliance to concordance: Achieving shared goals in medicine taking. London: Royal Pharmaceutical Society and Merck Sharp and Dohme; 1997.

McMillen S, Kelly F, Sav A, King MA, Whitty JA, Wheeler AJ. Australian community pharmacy services: A survey of what people with chronic conditions and their carers use versus what they consider important. British Medical Journal. 2014;4(12):8 pages.

Meigel W. How safe is oral isotretinoin? Dermatology. 1997;195(1):22-28.

Melton BL, Lai Z. Review of community pharmacy services: what is being performed, and where are the opportunities for improvement? Integrated Pharmacy Research and Practice. 2017;6:79-89.

Miller J. Iron deficiency anemia: A common and curable disease. Cold Spring Harbor Perspective in Medicine. 2013;3(7):13 pages.

Mitchell A, Van Bennekom C, Louik C. A pregnancy-prevention program in women of childbearing age receiving isotretinoin. New England Journal of Medicine. 1995;333(2):101-106.

Moffit K, Wassef C. Changes to NHS structure: how will it affect the future of pharmacy and you? Tomorrow's Pharmacist. 2014: 2 pages.

Montgomery AT, Kalvemark Sporrong S, Manap L, Tully MP, Lindbland AK. Receiving a pharmaceutical care service compared to receiving standard pharmacy service in Sweden - How do patients differ with regard to perceptions of medicine use and the pharmacy encounter? Research in Social and Administrative Pharmacy. 2010;6(3):185-195.

Moore T, Walsh C, Cohen M. Reported medication errors associated with methotrexate. American Journal of Health-System Pharmacy. 2004;61(13):1380-1384.

Moullin JC, Sabater-Hernandez D, Benrimoj SI. Qualitative study on the implementation of professional pharmacy services in Australian community pharmacies using framework analysis. BMC Health Services Research. 2016;16(1):439.

Moullin JC, Sabater-Hernandez D, Fernandez-Llimos F, Benrimoj SI. Defining professional pharmacy services in community pharmacy. Research in Social and Administrative Pharmacy. 2013;9(6):989-995.

Oforsi-Asenso R, Agyeman AA. Irrational use of medicines-A summary of key concepts. Journal of Pharmacy. 2016;4(35):13 pages.

Patel KV, Guralnik JM. Prognostic implications of anemia in older adults. Haematologica. 2009;94(1):1-2.

Pearson G. Evolution in the practice of pharmacy not a revolution! Canadian Medical Association Journal. 2007;176(9):1295-1296.

Perlman S, Leach E, Domunguez L, Ruszkowski A, Rudy S. "Be smart, be safe, be sure". The revised pregnancy prevention program for women on isotretinoin. The Journal of Reproductive Medicine. 2001;46(2):179-185.

Philipsen N. Regulation of and by pharmacists in the Netherlands and Belgium: An economic approach [Ph.D dissertation]. Maastricht: Maastricht University; 2003.

Philipsen N. Regulation of Pharmacists: A Comparative law and economics analysis. European Journal of Comparative Economics. 2014;10(2):225-241.

Pickering L, Wallace G, Rodewald L. Too hot, too cold: Issues with vaccine storage. Pediatrics. 2006;118(4):1738-1739.

Rademaker M. Adverse effects of isotretinoin: A retrospective review of 1743 patients started on isotretinoin. Australasian Journal of Dermatology. 2010;51(4):248-253.

Rapport F, Doel M, Hutchings H, Jerzembek G, John D, Wainwright P, et al. Through the looking glass: Public and professional perspectives on patient-centred professionalism in modern-day community pharmacy. Forum: Qualitative Social Research. 2010;11(1): 25 pages.

Russell J. The ASQ auditing handbook. Milwaukee, Wisconsin: ASQ Quality Press; 2013.

Sam A, Parasuraman S. The nine-star pharmacist: An overview. Journal of Young Pharmacists. 2015;7(4):281-284.

Sanchez-Ruiz M, Santos M, Jiménez J. The role of metaphorical thinking in the creativity of scientific discourse. Creativity Research Journal. 2013;25(4):361-368.

Sanz E. Concordance and children's use of medicines. British Medical Journal. 2003;327(7419):858-860.

Scicluna CA, Azzopardi LM, Serracino-Inglott A. Validation instruments for community pharmacy: An update. 1st ed. Germany: Lambert Academic Publishing; 2012.

Shapiro S, Rabinowitzs RS. Punishment versus cooperation in regulatory enforcement: A case study of OSHA. Administrative Law Review. 1997;49(4):714-762.

Shawahna R, Atrash A, Jebril A, Khalaf A, Shaheen E, Tahboosh H. Pharmacists' knowledge of issues in pharmacotherapy of epilepsy using antiepileptic drugs: A cross-sectional study in Palestinian pharmacy practice. Epilepsy and Behaviour. 2017;67:39-44.

Smith F. Research methods in pharmacy practice. London: Pharmaceutical Press; 2002.

Snowden A, Martin C, Mathers B, Donnell A. Concordance: A concept analysis. Journal of Advanced Nursing. 2013;70(1):46-59.

Stuchbery P, Kong DCM, Desaptis GN, Lo SK. Identification by observation of clinical pharmacists' activities in a hospital inpatient setting. Pharmacy Practice. 2007;5(1):10-16.

Taylor C. Education and personal development: A reflection. Archives of Disease in Childhood. 1999;81(6):531-537.

Thamby S, Subramani P. Seven-star pharmacist concept by World Health Organization. Journal of Young Pharmacists. 2014;6(2):1-3.

Trap B, Kikule K, Vialle Valentin C, Musoke R, Lajul G, Hoppenworth K, et al. First regulatory inspections measuring adherence to Good Pharmacy Practices in the public sector in Uganda: A cross-sectional comparison of performance between supervised and unsupervised facilities. Journal of Pharmaceutical Policy and Practice. 2016;9(1):10 pages.

Watson C. How concordance and patient empowerment challenge pharmacy. The Pharmaceutical Journal. 2009;271:494.

Weiss M, Britten N. What is concordance? The Pharmaceutical Journal. 2009;271:493.

Wiederholt J, Schommer J, Mount J, McGregor T, Braatz P. The Wisconsin pharmacy self-inspection project: An application of Berwick's theory of continuous improvement. American Journal of Pharmaceutical Education. 2002;66(1):27-36.

Wilcox G. Insulin and insulin resistance. The Clinical Biochemist Reviews. 2005;26(2):19-39.

Wirth F, Azzopardi LM, Serracino-Inglott A. Quality management system for clinical pharmacy services. Saarbrücken: Scholar's Press; 2013.

Wood S. Aristotle and the question of metaphor [Ph.D dissertation]. Canada: University of Ottawa; 2015.

Wubante DN. Patient counselling at dispensing of medicines in health care facility outpatient pharmacies of Bahir Dar city, Northwest Ethiopia. Science Journal of Public Health. 2014;2(2):126-134.

Yavari P, Etemad K, Haghdoodt A, Mehrabi Y, Motlagh M, Kabir M, et al. Inequality in utilization of in-patients health services in Iran. International Journal of Preventive Medicine. 2015;6(1):45.

Appendix 1

Updates to the community pharmacy regulatory audit tool and rationale for the update

Table A1:

Updated audit tool features	Rationale
Administrative data **Omitted;** unnecessary data collection including address of pharmacy, license holder details **Added;** section B to account for any changes in pharmacy license details (address and license holder details); section C including private contact details of the managing pharmacist; section D including contact details of the locum pharmacist	Concerning the administrative data section, the address of the pharmacy and license holder details were omitted since this data is readily available at MMA. The addition of Section B of the audit tool was suggested by the IED Director before implementing changes to cover for any unforeseen changes in the pharmacy license. Section C and D were added to have direct access to the pharmacists involved in the audit.
(New) Added: section F, subsection 1: **Checking for SOPs**	The rationale behind addition of this subsection are feedback from the interviews with the community pharmacists, allowing for checking for implementation of SOPs during the CPRA.
Added: section F, subsection 2: **Storage of medicinal products**	This subsection combined 4 scattered points from the past audit tool; temperature monitoring, thermometer calibration, condition of medicines and refrigerator use. From the retrospective analysis a high percentage of CPRA reports indicated problems with regards to temperature issues, and feedback from the interviews with the community pharmacists suggested ensuring appropriate temperature monitoring. This subsection was expanded to include storage of POMs, capacity of refrigerator, AC service and checking for an expiry management system. The temperature monitoring questions included: monitoring POYC stock areas and any additional storage; and monitoring of minimum and maximum temperatures.

Updated audit tool features	Rationale
Added: section F, subsection 3: **Locum register and the pharmacist**	This subsection of the updated audit tool groups together 3 scattered points from the past audit tool which relates to the pharmacist. The retrospective analysis indicated that pharmacists were not always wearing the white coat and pharmacy council badge. The interviews with the community pharmacists suggested ensuring that the patient is attended to by a pharmacist and not by non-pharmacists, and appearance was deemed as key to allow the patient to recognise the pharmacist. The locum register was included under this subsection.
Added: section F subsection 4: **Daily dispensing register**	All records incorporated under relevant subheading and not scattered. From the interviews with the community pharmacists it was identified that the majority of pharmacists complained of register upkeep, hence the option of keeping registers electronically, either by keeping a soft copy or by scanning the prescriptions (for the daily and DDA registers) was introduced. This was carried out with the aim to reduce the burden from keeping registers updated only for audit purposes and with the aim to reduce workload and 'lost' time updating registers, allowing the community pharmacist to spend more time interacting with the patient providing pharmaceutical care. The upkeep of registers was not omitted since the retrospective analysis showed registers are not always kept in order. This change applied for all registers available at the pharmacy; locum, daily, DDA sales, DDA purchases, cleaning records and temperature records registers.

Updated audit tool features	Rationale
From the DDA section of the previous CPRA tool **Omitted:** the checking of green prescriptions **Added:** -section F subsection 5: **DDA registers section** -section F subsection 6: **DDA stock take** -section F subsection 7: **DDA cupboard**	All records incorporated under relevant subheading and not scattered. The checking of green prescriptions was omitted, since from the retrospective analysis it was identified that for 5 years this was always found to be in accordance with legislation. For stock take of DDAs, the practice of sending it yearly to the MMA was changed and instead it will be checked during the CPRA. Headings to be used for stock take were suggested. DDA cupboard section expanded to include checking for segregation of expired DDAs and assessing whether the cupboard permits the orderly storage of DDAs and distinguishing between having the cupboard but not kept locked.
From the extemporaneous preparation section in the previous CPRA tool **Omitted:** grading the condition of the utensils as fair/good/excellent **Added:** section F subsection 8; **extemporaneous section optional**; included a list of the required utensils, and the checking for dedicated areas and labelling materials	An old practice is the need to keep the full range of utensils for extemporaneous preparations. Analysing the utensils to grade whether they are of fair, good or excellent condition was omitted. Nowadays, only a small percentage of pharmacies still prepare extemporaneous medicines. In the updated CPRA tool, the extemporaneous preparations section is optional. Only graduated cylinders and tablet counters are required for daily pharmacy services.
Condition of medicine section from previous tool **Omitted:** checking invoices at pharmacy Refrigerator use and condition of medicine moved under storage of medicinal products.	From the retrospective analysis, it was noted that buying from authorised wholesale dealers was always found to be in accordance with legislation for the past 5 years, hence checking of invoices during the CPRA was omitted. Refrigerator use and condition of medicine was moved under storage of medicinal products to increase relevance.

Updated audit tool features	Rationale
Conditions of premises expanded under section F subsection 9 **Omitted:** grading of the condition of premises as fair/good/excellent **Retained:** cleaning records and pest control **Added:** security arrangement, checking state of repair, maintenance of entrances, dispensing bench, toilet facilities	All records incorporated under relevant subheading and not scattered. Grading of the condition of premises was omitted. Instead, condition of premises was expanded in this subsection, joining 3 scattered points; condition, cleaning records and pest control certificate. A suggestion from the interviews with the community pharmacists was to ensure that pharmacies are safe and are easily accessible. Addition of new questions included; checking the state of repair and accessibility to the pharmacy.
Added (new): Section F subsection 10: **Miscellaneous section**; reference books, sharps bin, segregation of waste	A miscellaneous subsection covering feedback from the interviews with the community pharmacists to improve professional pharmacy services, included the addition of checking for reference books and sharps bin for POCT. Included the checking for segregation of expired medicine to ensure that expired medicines are not dispensed to patients.
Signature section **Retained from previous tool:** but separated in 2 sections; section E, signature of pharmacist and section G, signature of auditors	N/A

Appendix 2

The community pharmacy regulatory audit tool

Tool for a CPRA by the Medicines Authority of Malta

A. Dispensary Details:

i. **Name:**

ii. **Locality:**

iii. **Email address:**

iv. **Telephone number:**

B. Change in pharmacy license details:

	YES	NO
Any change in pharmacy address? **If yes, enter details;**		
Any change in license holder/ address? **If yes, enter details;**		

C. Name, registration number and contact details of the managing pharmacist*:

i. **Name:**

ii. **Registration number:**

iii. **Mobile number:**

D. *If the managing pharmacist is not present, what is the name and registration number of the locum pharmacist present at the audit?

i. **Name:**

ii. **Registration number:**

E. Managing/ locum pharmacist signature: _____

F. Checklist:

1	**Standard Operating Procedures**	**YES**	**NO**	**COMMENTS** *(where applicable)*
1.1	Is the pharmacy equipped with SOPs? *If yes, comment which SOPs are available*			
2	**Storage of Medicinal Products** *Medicines Act Chapter 458 Article 85 (1) and (2)* *Medicines Act Chapter 458 Article 86*	**YES**	**NO**	**COMMENTS** *(where applicable)*
2.1	Are all medicines stored in an area of the pharmacy under the control of the pharmacist?			
2.2	Is the fridge clean with only medicinal products stored within?			
2.3	Are all medicines stored in the fridge in good condition?			
2.4	Is the fridge of an adequate capacity to permit the orderly storage of medicines? *Comment: pharmaceutical grade fridges recommended*			
2.5	Are the thermometers calibrated annually? **Certificate number:-** _____			
2.6	Is the air conditioner serviced annually? **Certificate number:**_____			
2.7	Is the maximum/minimum **fridge temperature for the pharmacy stock** monitored, recorded and reviewed on a daily basis as per the Medicines Act Guidelines on the Storage of Medicinal Products within a Pharmacy?			
2.8	Is the maximum/minimum **fridge temperature for the POYC stock** (if applicable) monitored, recorded and reviewed on a daily basis as per the Medicines Act Guidelines on the Storage of Medicinal Products within a Pharmacy?			

2.9	Is the maximum/minimum **temperature in the dispensary and any additional storage areas for pharmacy stock** monitored, recorded and reviewed on a daily basis as per the Medicines Act Guidelines on the Storage of Medicinal Products within a Pharmacy?			
2.10	Is the maximum/minimum **temperature in the dispensary and any additional storage areas for POYC stock** (if applicable) monitored, recorded and reviewed on a daily basis as per the Medicines Act Guidelines on the Storage of Medicinal Products within a Pharmacy?			
2.11	Are all medicines stored in the pharmacy in date and is there an active documented expiry date management system in place? *Medicines Act Chapter 458 Article 84 (b)*			
3	**Locum Register and the Pharmacist**	**YES**	**NO**	**COMMENTS** *(where applicable)*
3.1	Is there a pharmacist supervising the pharmacy for all hours of opening and is this recorded in the locum register (excludes managing pharmacist)? *Medicines Act Chapter 458 Article 74 (g)* *Medicines Act Chapter 458 Article 75 (2)(b)*			
3.2	Is the pharmacist wearing a white coat while attending to his professional duties? *Medicines Act Subsidiary Legislation 458.16 Article 13 (3)*			
3.3	Does the pharmacist have the identity tag issued by the Pharmacy Council attached to his coat? *Medicines Act Chapter 458 Subsidiary Legislation 16 Article 13 (3)*			
4	**Daily Dispensing Registers** *Medicines Act Chapter 458 Article 86*	**YES**	**NO**	**COMMENTS** *(where applicable)*
4.1	Is the prescription register/ daily dispensing report recorded on a daily basis?			

4.2	Daily dispensing report being scanned? *Medicines Act Chapter 458 Subsidiary Legislation 49 Article 6 (2)*			
4.3	Is the prescription register/ daily dispensing report completed in the correct format in accordance with the requirements of Article 6 of the Subsidiary Legislation 458.49 (Prescription and Dispensing Requirements Rules) (as amended)? *(date on which the prescription is dispensed, name, quantity and the pharmaceutical form and strength of the product, full name of the prescriber and his registration number, date of the prescription, in the case of medicinal products dispensed in compliance with rule 4(3), the date on which the prescription is received)*			
4.4	Are all prescriptions for the previous three months available for review at the premises? *Medicines Act Subsidiary Legislation 458.16 Article 12 (2)*			
5	**Dangerous Drug Registers** *Dangerous Drugs Ordinance Subsidiary Legislation 101.02 Article 11*	**YES**	**NO**	**COMMENTS** *(where applicable)*
5.1	Is the **Dangerous Drug Sales register for pharmacy stock** kept updated? (Within 1 month limit)			
5.2	Is the **Dangerous Drug Purchases register for pharmacy stock** kept updated? (Within 1 month limit)			
5.3	Is **Dangerous Drug Sales register for POYC** kept updated? (Within 1 month limit)			
5.4	Is the **Dangerous Drug Purchases register kept updated and are invoices kept in an orderly manner for POYC**? (Within 1 month limit)			
5.5	Are both dangerous drugs registers from the last audit available for review?			

5.6	Is the Dangerous Drug Sales Register completed in the correct format in accordance with the requirements of Article 6 of the Subsidiary Legislation 458.49 (Prescription and Dispensing Requirements Rules) (as amended)? *(date on which the prescription is dispensed, name, quantity and the pharmaceutical form and strength of the product, full name of the prescriber and his registration number, date and number of the prescription, in the case of medicinal products dispensed in compliance with rule 4(3), the date on which the prescription is received)*			
5.7	Where dangerous drugs have been removed from the active balance, either because they are expired or destroyed is there documentation available?			
6	**Dangerous Drug Stock Take**	**YES**	**NO**	**COMMENTS** *(where applicable)*
6.1	Is a stock taking exercise carried out yearly and report sent to Medicines Authority? Stock take report headings minimum requirement: Stock level of previous year, Quantity Procured, Quantity Dispensed, Quantity, Quantity Expected and Actual Stock Level *Dangerous Drugs Ordinance Subsidiary Legislation 101.02 Article 11 (g)*			
7	**Dangerous Drug Cupboard** *Dangerous Drugs Ordinance Subsidiary Legislation 101.02 Article 12 (2)*	**YES**	**NO**	**COMMENTS** *(where applicable)*
7.1	Is there a lockable cabinet for the storage of narcotic and psychotropic substances in place in the dispensary?			
7.2	Is the key kept solely and all the time by the managing pharmacist?			

7.3	Does the Dangerous Drug cabinet have sufficient capacity to permit the orderly storage of all dangerous drugs?			
7.4	Are all narcotic and psychotropic substances stored in the dangerous drug safe? Is the cabinet reserved solely for the storage of medicines?			
7.5	Are expired/ patient returned dangerous drugs stored in a designated part of the DDA cupboard and appropriately labelled? *Medicines Act Chapter 458 Article 84* *Medicines Act Subsidiary Legislation 458.16 Article 9 (k)*			
8	**EXTEMPORANEOUS PREPERATIONS**	**YES**	**NO**	**COMMENTS** *(where applicable)*
8.1	Are extemporaneous preparations carried out at the pharmacy?			
If yes, go to 8.2, if not go to 8.9				
8.2	Are preparations labelled with all information required in accordance with regulations or rules made under the Medicines Act? *Comment: Expiry date of 4 weeks for all extemporaneous preparations* *Medicines Act Chapter 458 Article 83* *Medicines Act Chapter 458 Article 87*			
8.3	Are dedicated areas for preparing Extemporaneous Products in place? *Medicines Act Subsidiary Legislation 458.16 Article 9 (e)*			
8.4	Is all required equipment available in the pharmacy? *Medicines Act Chapter 458 Article 86* *Medicines Act Chapter 458 Article 87*			
8.5	Electronic balance (accurately measures 0.1g to 200g)			

8.6	Ointment glass/marble slab			
8.7	Spatulas & stirrers			
8.8	Mortars and pestles			
8.9	Graduated cylinders			
8.10	Tablet counter			
8.11	Is all equipment kept in a clean state?			
9	**Premises**	**YES**	**NO**	**COMMENTS** *(where applicable)*
9.1	Display box available for displaying Sunday roster? *Medicines Act Subsidiary Legislation 458.16 Article 13 (4)*			
9.2	Are there adequate security arrangements in place, e.g. alarm, shutters, CCTV, glass thickness (minimum 10mm), iron bars as applicable? *Medicines Act Subsidiary Legislation 458.16 Article 9 (i)*			
9.3	Are the **external and internal** premises in a good state of repair and decoration, and are all fixtures and fittings of an acceptable standard? *Medicines Act Subsidiary Legislation 458.16 Article 10*			
9.4	Are all entrances to the premises well maintained, clear and accessible? *Medicines Act Subsidiary Legislation 458.16 Article 9 (a)*			
9.5	Is the trading name of the pharmacy displayed at all entrances to the premises? *Medicines Act Subsidiary Legislation 458.16 Article 9 (b)*			
9.6	Is a dispensing bench with a smooth impervious & washable surface and adequate space for expected volume of activity in place? *Medicines Act Subsidiary Legislation 458.16 Article 9 (c)*			

9.7	Is there a dedicated dispensary sink/dispenser with access to hot and cold (potable) water? *Medicines Act Subsidiary Legislation 458.16 Article 9 (b)*			
9.8	Is adequate lighting/ ventilation provided in the dispensary? *Medicines Act Subsidiary Legislation 458.16 Article 9 (g)*			
9.9	Is access to the dispensary and all areas where medicines or confidential records are stored restricted to authorised personnel?			
9.10	Is there a clean and well maintained toilet and wash hand basin provided at the premises? *Medicines Act Subsidiary Legislation 458.16 Article 9 (j)*			
9.11	Is housekeeping in all areas of the pharmacy maintained at an acceptable standard and is a cleaning register countersigned by the managing pharmacist and kept in an orderly manner? *Medicines Act Subsidiary Legislation 458.16 Article 9 (d)*			
9.12	Is pest control done annually to all areas of the pharmacy? **Certificate number:_____**			
10	**Miscellaneous**	**YES**	**NO**	**COMMENTS** *(where applicable)*
10.1	Does the pharmacy have appropriate and up to date reference books? (Recommended BNF within 2 year of issue and Maltese Medicine Handbook) *Medicines Act Subsidiary Legislation 458.16 Article 11* *Specify title and issue date:*			

10.2	Does the pharmacy have a medicinal product waste bin, and sharp objects bin? *Medicines Act Chapter 458 Article 84* *Medicines Act Subsidiary Legislation 458.16 Article 9 (k)*			
10.3	Is all waste and patient returned medication stored in a designated area of the pharmacy segregated from active stock pending timely processing? *Medicines Act Chapter 458 Article 84* *Medicines Act Subsidiary Legislation 458.16 Article 9 (k)*			

G. Auditors signatures and date:

Appendix 3

List of medicines identified and stability implications

(case study 6)

Table A2:

Trade name (dosage form)	Quantity
Actrapid 100IU/ml solution for injection (in vials)	12
Avonex 30mcg/0.5ml solution for injection (in pre filled pen)	16
Eporatio 4,000IU/0.5ml solution for injection (in pre-filled syringe)	4
Glucagen 1mg (powder and solvent) for solution for injection	7
Humulin I 100IU/ml suspension for injection (in cartridge)	58
Humulin M3 100IU/ml suspension for injection (in cartridge)	36
Humulin S 100IU/ml solution for injection (in cartridge)	28
Insulatard 100IU/ml suspension for injection (in vials)	23
Lantus Solostar 100IU/ml solution for injection (in a pre-filled pen)	9
Mixtard 30 100IU/ml suspension for injection (in vials)	19
Novorapid Penfill 100IU/ml for injection (in cartridge)	26
Nuvaring (vaginal device)	1
Ovitrelle 250mcg/0.5ml solution for injection (in pre-filled pen)	1
Prolia 60mg solution for injection (in pre-filled syringe)	2
Varilrix (vaccine)	1
Vaxigrip influenza (vaccine)	8

Table A3:

References

Amgen Ltd. Prolia - Summary of Product Characteristics [Online]. UK: eMc; 2017 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/product/568

Biogen Idex Ltd. Avonex - Summary of Product Characteristics [Online]. UK: eMC; 2017 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/product/4649/smpc

Hamborsky J, Kroger A, Wolfe C. Epidemiology and prevention of vaccine-preventable diseases. 13th ed. Washington DC: Public Health Foundation; 2015.

Eli Lilly and Company Limited. Humulin I (Isophane) 100IU/ml suspension for injection in cartridge- Summary of Product Characteristics [Online]. UK: eMC; 2017 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/product/8195/smpc

Eli Lilly and Company Limited. Humulin M3 (Mixture 3) 100IU/ml suspension for injection in cartridge- Summary of Product Characteristics [Online]. UK: eMC; 2017 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/product/8192/smpc

Eli Lilly and Company Limited. Humulin S (Soluble) 100IU/ml suspension for injection in cartridge- Summary of Product Characteristics [Online]. UK: eMC; 2017 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/product/8197/smpc

European Medicines Agency. Actrapid European Public Assessment Report [Online]. London: European Medicines Agency; 2013 [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/000424/WC500021653.pdf

European Medicines Agency. Avonex European Public Assessment Report [Online]. London: European Medicines Agency; 2011 [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/000102/WC500029423.pdf

European Medicines Agency. Eporatio European Public Assessment Report [Online]. London: European Medicines Agency; 2009 [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR__Summary_for_the_public/human/001033/WC500043301.pdf

European Medicines Agency. Insulatard European Public Assessment Report [Online]. London: European Medicines Agency; 2014 [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR__Summary_for_the_public/human/000441/WC500033303.pdf

European Medicines Agency. Mixtard European Public Assessment Report [Online]. London: European Medicines Agency; 2014 [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/000428/WC500029817.pdf

European Medicines Agency. Novorapid European Public Assessment Report [Online]. London: European Medicines Agency; 2016 [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/000258/WC500030368.pdf

European Medicines Agency. Ovitrelle European Public Assessment Report [Online]. London: European Medicines Agency; 2011 [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/000320/WC500051447.pdf

European Medicines Agency. Prolia European Public Assessment Report [Online]. London: European Medicines Agency; 2015 [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/001120/WC500093527.pdf

GlaxoSmithKline. Varilrix vaccine - Summary of Product Characteristics [Online]. UK: eMC; 2017 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/product/1676/smpc

Merck Sharp and Dohme Ltd. Nuvaring - Summary of Product Characteristics [Online]. UK: eMC; 2018 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/product/6449

Merck. Ovitrelle 250 micrograms/0.5 ml prefilled pen - Summary of Product Characteristics [Online]. UK: eMc; 2014 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/product/2806/smpc

National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases. Chickenpox (Varicella) [Online]. USA: Centres for Disease Control and Prevention. 2016 [cited 2018 May 30]. Available from: URL: https://www.cdc.gov/chickenpox/about/index.html

Novo Nordisk. Mixtard 30 100IU/ml suspension for injections in vials - Summary of Product Characteristics [Online]. UK: EMA; 2007 [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000428/WC500029822.pdf

Novo Nordisk. NovoRapid Penfill 100 units/ml - Summary of Product Characteristics [Online]. UK: eMc; 2017 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/product/4779/smpc

NovoNordisk. Actrapid - Summary of Product Characteristics [Online]. UK: eMC; 2018 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/product/3849/smpc

NovoNordisk. GlucaGen Hypokit 1mg - Summary of Product Characteristics [Online]. UK: eMC; 2015 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/product/1289/smpc

NovoNordisk. Insulatard 100IU/ml - Summary of Product Characteristics [Online]. UK: eMC; 2018 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/product/3848/smpc

Ratiopharm. Eporatio - Summary of Product Characteristics [Online]. UK: EMA; 2014 [cited 2018 May 30]. Available from: URL: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/001033/WC500043300.pdf

Sanofi Pasteur. Inactivated influenza vaccine (Split virion BP) - Summary of Product Characteristics [Online]. UK: eMC; 2018 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/product/1395/smpc

Sanofi Pasteur. Lantus 100 Units/ml solution for injection in SoloStar pre-filled pen- Summary of Product Characteristics [Online]. UK: eMC; 2018 [cited 2018 May 30]. Available from: URL: https://www.medicines.org.uk/emc/product/8098/smpc

World Health Organization. Aide-Memoire for prevention of freezing damage to vaccines [Online]. Geneva: WHO. 2009 [cited 2018 May 30]. Available from: URL: http://apps.who.int/iris/bitstream/handle/10665/69673/WHO_IVB_07.09_eng.pdf?sequence

Appendix 4

Dissemination of results in international fora

Abstract accepted for poster presentation at the International Pharmaceutical Federation World Congress of Pharmacy and Pharmaceutical Sciences, Glasgow, Scotland, September 2018

REACHING CONCORDANCE IN COMMUNITY PHARMACY REGULATORY AUDITS

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Background

Pharmacy practice is evolving to incorporate a patient-centred approach to the scientific background. Pharmacy audits reaching concordance between the practicing pharmacist and the auditor to the benefit of the patient are envisaged.

Purpose

To develop and implement a tool for community pharmacy regulatory audits (CPRAs) and identify case studies from CPRAs to recommend improvements to patient safety.

Method

An audit tool for CPRAs was developed and implemented in 85 routine CPRAs (January-November 2017) and desirable patient-related improvements were identified through informal educational discussions with the practicing pharmacists. Seven case studies on the identified deficiencies related to patient safety were addressed.

Results

The seven case studies identified are: one equity of treatment between private and government-sponsored patients, four dispensing problems (errors, near misses, lack of proper prescription, unsupervised pharmacy staff) and two inventory deficiencies (expired items, inappropriate temperature storage). Concordance with the pharmacist was reached and actions taken to address the deficiencies. Standard operating procedures were developed, such as for temperature recording, identifying who is responsible for the procedure and keeping of records, supervision was to be recorded, rotation and records of expiry dates with methods for alerts were devised and methods to communicate with patients, including when a possible error is detected, were identified.

Conclusion

Follow-up audits confirmed that reaching concordance to regulation through implementation of an educational approach should improve pharmacist motivation and patient care outcomes.

Abstract accepted for poster presentation at the American College of Clinical Pharmacy Global Conference on Clinical Pharmacy, Seattle, USA, October 2018

PATIENT-CENTRED REGULATORY AUDITS IN COMMUNITY PHARMACY

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Introduction

The patient is not central to regulatory audits of community pharmacy. The Malta Medicines Authority, which regulates community pharmacies, is considering a patient-centred approach in its audits to reach concordance between the practicing pharmacist and the regulator.

Research Question

Can concordance in community pharmacy regulatory audits (CPRAs) lead to optimised patient-centred practice?

Study Design

Qualitative and quantitative study design

Methods

Reports from 512 CPRAs for a 57-month period were retrospectively analysed to extract features that could lead to identification of patient-related deficiencies in community pharmacy practice. A validated audit tool was developed by conducting interviews with 12 community pharmacists and by analysing the retrospective data. The tool was implemented in 85 routine CPRAs from January to November 2017 and desirable patient-related improvements were identified through informal educational discussions with the practicing pharmacists. Case studies on the identified deficiencies related to patient safety were evaluated through review of dossiers, European Public Assessment Reports and consultation with the Marketing Authorisation Holders.

Results

Storage of insulins, vaccines and epoetins below 2℃ presented an example of a case study which could threaten intended therapeutic outcomes. Dispensing of government-paid prescriptions being given secondary importance versus private prescriptions formed the basis of another case study. Concordance was reached to ensure that equal attention is given to all patients. A reported complaint of an error of dispensing methotrexate 2.5mg instead of methyldopa 250mg was followed up by an audit to find a possible cause for dispensing errors. Concordance between the auditor and the pharmacist was reached to store cytotoxic drugs in a separate cabinet as a corrective action.

Conclusions

An educational approach by the auditor reaching concordance to regulation as distinct from punitive enforcement may improve pharmacist motivation and patient care outcomes.

Trade name (active ingredient)	Visual appearance of the product	Storage conditions	Allowed excursions	Stability implications	Source of information
Actrapid 100IU/ml solution for injection in vials (Human Insulin)	Clear, colourless and aqueous solution	2°C to 8°C Do not freeze Actrapid® which has been frozen must not be used	Actrapid® has excellent stability for 42 days below 25°C	No stability studies performed below 2°C. Stability studies are satisfactory documented for a shelf life of 30 months when stored at 5°C +/-3°C.	Dossier Contacted MAH EPAR SPC
Avonex 30mcg/0.5ml solution for injection in pre filled pen (Interferon beta 1alfa)	Clear and colourless solution	2°C to 8°C Do not freeze	Stable at room temperature (between 15°C to 30°C) for 7 days	No stability studies performed below 2°C. Stability studies support shelf life of 36 months when stored at 5°C +/- 3°C.	Dossier Contacted MAH EPAR SPC
Eporatio 4,000IU/0.5ml solution for injection in pre-filled syringe (Epoetin theta)	Clear and colourless solution	2°C to 8°C Do not freeze	It is suggested that it is stored for 7 days only below 25°C, and that it must be used within this period or else discarded	No stability studies performed below 2°C. Oxidation of epoetin theta was faster but without a negative impact on stability, when stored for 4 weeks at 25°C +/- 2°C. Biological activity remained the same for 24 months stored at 5°C +/- 3°C.	Dossier Contacted MAH EPAR SPC

Trade name (active ingredient)	Visual appearance of the product	Storage conditions	Allowed excursions	Stability implications	Source of information
Glucagen 1mg powder and solvent for solution for injection (Human glucagon)	Powder and solvent for solution Powder: white/ nearly white Solvent: clear and colourless without particles	2°C to 8°C Do not freeze	Glucagen Hypokit can be stored below 25°C for 18 months	No stability studies performed below 2°C. Stability studies are satisfactory documented for a shelf life of 36 months when stored at 5°C +/-3°C, prior to reconstitution, hereof 18 months can be at maximum of 25°C.	Dossier Contacted MAH SPC
Humulin I 100IU/ml suspension for injection in cartridge (Isophane human insulin)	Cloudy, white and aqueous suspension	2°C to 8°C Do not freeze	28 days at 30°C	No stability studies performed below 2°C. Accelerated stability studies at 30°C allows an excursion at this temperature for 28 days. Stability studies are satisfactory documented for a shelf life of 36 months when stored at 5°C +/-3°C	Dossier Contacted MAH SPC

Trade name (active ingredient)	Visual appearance of the product	Storage conditions	Allowed excursions	Stability implications	Source of information
Humulin M3 100IU/ml suspension for injection in cartridge (Mixture 3 human insulin)	Cloudy, white and aqueous suspension	2°C to 8°C Do not freeze	28 days at 30°C	No stability studies performed below 2°C. Accelerated stability studies at 30°C allows an excursion at this temperature for 28 days. Stability studies are satisfactory documented for a shelf life of 36 months when stored at 5°C +/-3°C	Dossier Contacted MAH SPC
Humulin S 100IU/ml solution for injection in cartridge (Soluble human insulin)	Clear, colourless, aqueous solution	2°C to 8°C Do not freeze	28 days at 30°C	No stability studies performed below 2°C. Accelerated stability studies at 30°C allows an excursion at this temperature for 28 days. Stability studies are satisfactory documented for a shelf life of 24 months when stored at 5°C +/-3°C	Dossier Contacted MAH SPC

Trade name (active ingredient)	Visual appearance of the product	Storage conditions	Allowed excursions	Stability implications	Source of information
Insulatard 100IU/ml suspension for injection in vials (Human Insulin)	Cloudy, white and aqueous suspension	2°C to 8°C Do not freeze	Insulatard® has excellent stability for 42 days below 25°C	No stability studies performed below 2°C. Stability studies are satisfactory documented for a shelf life of 30 months when stored at 5°C +/-3°C.	Dossier Contacted MAH EPAR SPC
Lantus Solostar 100IU/ml solution for injection in a pre-filled pen (Insulin glargine)	Clear, colourless solution	2°C to 8°C Insulin glargine should not be stored in the freezer, near the freezer compartment or a freezer pack, and should be discarded if frozen	Lantus® has excellent stability for 28 days below 30°C	No stability studies performed below 2°C. Stability studies support a shelf life of 36 months when stored at 2°C to 8°C.	Dossier Contacted MAH SPC
Mixtard 30 100IU/ml suspension for injection in vials (Human insulin/ isophane human insulin)	Cloudy, white and aqueous suspension	2°C to 8°C Do not freeze	Mixtard 30® has excellent stability for 42 days below 25°C	No stability studies performed below 2°C. Stability studies are satisfactory documented for a shelf life of 30 months when stored at 5°C +/-3°C.	Dossier Contacted MAH EPAR SPC

Trade name (active ingredient)	Visual appearance of the product	Storage conditions	Allowed excursions	Stability implications	Source of information
Novorapid Penfill 100IU/ml for injection in cartridge (Insulin aspart)	Clear, colourless and aqueous solution	2°C to 8°C Do not freeze	Novorapid® has excellent stability for 28 days below 30°C	No stability studies performed below 2°C. Stability studies shows satisfactory physical and chemical stability for a shelf life of 30 months when stored at 5°C +/-3°C.	Dossier Contacted MAH EPAR SPC
Nuvaring (0.120mg ethinylestradiol/0.015mg etonogestrel)	Flexible, transparent, and colourless to almost colourless ring	2°C to 8°C	Nuvaring® remains stable at 2°C to 8°C for 37 months, at up to 30°C for 13 months, and up to 40°C for 6 months.	No stability studies performed below 2°C. Studies showed that it is chemically, physically, mechanically and microbial sufficiently stable during storage at 2°C to 8°C for a period of 37 months and at 2°C to 8°C for at least 24 months followed by 13 months of storage up to 25°C and 30°C. It is also stable under accelerated condition of 40°C for at least 6 months.	Dossier Contacted MAH SPC

Trade name (active ingredient)	Visual appearance of the product	Storage conditions	Allowed excursions	Stability implications	Source of information
Ovitrelle 250mcg/0.5ml solution for injection in pre-filled pen (Choriogonadotropin alfa)	Clear, colourless to slightly yellow solution	2°C to 8°C Do not freeze	It may be stored at or below 25°C for up to 30 days. Ovitrelle can be allowed to reach up to -20°C for not more than 72 hours.	Stable for up to 30 days at temperatures of 25°C and below. Stability studies shows satisfactory physical and chemical stability for a shelf life of 24 months when stored at 5°C +/-3°C.	Dossier Contacted MAH EPAR SPC
Prolia 60mg solution for injection in pre-filled syringe (Denusomab)	Clear, colourless to slightly yellow solution	2°C to 8°C Do not freeze	Stable below 25°C for 30 days	Stability studies not performed below 2°C. Prolia showed satisfactory stability results when stored below 25°C for up to 30 days. Stability studies shows satisfactory physical and chemical stability for a shelf life of 30 months when stored at 5°C +/-3°C.	Dossier Contacted MAH EPAR SPC

Trade name (active ingredient)	Visual appearance of the product	Storage conditions	Allowed excursions	Stability implications	Source of information
Varilrix Vaccine **(Live attenuated Varicella zoster virus)**	Cream to yellowish or pinkish coloured powder and solvent for reconstitution	2°C to 8°C Do not freeze	Stability data shows that it can be administered following excursions between 2°C and -25°C. A maximum cumulative period of 72 hours is permitted for the vaccine to be stored between 8°C through 25°C, however only for administration reasons and not for temperature excursions at the pharmacy.	Varilrix® is a lyophilised vaccine, thus it stable frozen above -25°C. However, once thawed, temperature recycling can affect stability, and thus should not be refrozen. Diluent should not be frozen. Stability studies shows satisfactory physical and chemical stability for a shelf life of 24 months when stored at 5°C +/-3°C.	Dossier Contacted MAH Centers for Disease Control and Prevention, 2015 CDC SPC
Vaxigrip influenza vaccine **(Inactivated influenza vaccine BP)**	Suspension, becoming whitish and opalescent liquid after shaking	2°C to 8°C Do not freeze	None	Vaxigrip® vaccine is only stable for 12 months. No stability studies carried out above 8°C or below 2°C.	Dossier Aide-Memoire WHO SPC