

**T.R.N.C**  
**NEAR EAST UNIVERSITY**  
**INSTITUTE OF HEALTH SCIENCES**

**Introducing Clinical Pharmacy Services:  
Efficacy in a Respiratory Diseases Clinic and Physicians  
Perceptions toward the Service at NEU Hospital  
in Northern Cyprus.**

**A THESIS SUBMITTED TO THE GRADUATE INSTITUTE OF  
HEALTH SCIENCES**

**BY:**  
**Abdikarim Mohamed Abdi**

**In Partial Fulfillment of the Requirements for the Degree of  
Master of Science in Clinical Pharmacy**

**NICOSIA 2014**

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**Master of Science in Clinical Pharmacy**

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## ACKNOWLEDGEMENT

**Alhamdulillah**, First and foremost, thanks Allah Almighty for endowing me with patience, and knowledge to complete this achievement. Special thanks are for the faculty of pharmacy at NEU, and its deanship for their support giving me the opportunity to pursue my graduate studies in their honorable faculty. I acknowledge and deeply appreciate **Prof.Dr. Rümeysa Demirdamar**, my major advisor and mentor for her support and encouragement throughout my study at NEU and during each step of this work allowing me to become a research scientist in clinical pharmacy practice.

I owe my deepest gratitude and much respect to **Prof.Dr. Finn Rasmussen** my co –adviser, for his valuable time, inspiration, encouragement, and guidance given to me during my training and research time, **Dr Rasmussen** good advice, support and friendship was priceless on both academic and personal levels and meant a lot for me being more than an adviser or a teacher, also this thesis would not have been possible without his guidance and patience. I am also grateful to **Prof. Rushtu Onur** and **Prof. Shahan Saygi**, my professors and jury committee members, for their cooperation during the study period and constructive guidance, valuable advice and encouragement, also **Prof. Bahar Tunchtan & Prof. Ichlal** deserve many thanks for their support during the preparatory period of the thesis. I also acknowledge the invaluable efforts and cooperation of healthcare team including physicians, nurses & secretary at the **Respiratory & Allergic Diseases Clinic**, of NEU Hospital, and also my colleague pharmacists at the hospital's pharmacy **Ashfaq** who helped and well cooperated with me during my work and **Onur** for his aid in Turkish translation.

Deep thanks are to my friend and teacher **Prof. Wesam Ismail** from Jordan who kept in close contact, and gave valuable consults during my work and study, also acknowledgment is due to **Eng. Ahmed Farajallah** my room-mate during my work, who gave me much encouragement during the writing phase and also in obtaining valuable materials which I used during my work, I deeply appreciate his help and also presence during my jury, and account him as a big brother more than a friend.

I must also thank all my professors at my master degree in **Near East University**, beside my teachers and professors during my undergraduate Pharm.D degree at **Jordan University of Science and Technology** who really owe majority of the credit for my knowledge and professionalism and kept in contact with me since my graduation and up today, supporting and encouraging, them and all my friends & colleagues from **JUST** university and **Jordan** I really and deeply appreciate and acknowledge their generosity and encouragement.

Also many thanks are for **Eng. Ashraf Awad**, and my aunt **Shukri** & her husband **Prof.Dr. Abdurrahman**, who because of their consult I came to Turkey & TRNC for obtaining my graduate degree.

Finally, I would like to express my deepest heartfelt gratitude to **my lovely mother, my father who mentored me**, brothers **Abdurrahman & Abdulla**, sisters, future wife ☺, grandma's, aunties, uncles and all other relatives, for their emotional and moral support throughout my academic career and also for their prayers.

## **ABSTRACT**

**Abdikarim M.abdi, Introducing clinical pharmacy services: efficacy in a RD clinic and physicians perceptions toward the services at NEU Hospital in Northern Cyprus. Near East University, Institute of Health Sciences, Clinical Pharmacy Master's Thesis', Nicosia, 2014.**

Clinical pharmacists are a primary source of scientifically valid information and advice regarding the safe, appropriate, and cost-effective use of medications having wide scope in drug Information and utilization, After the introduction of the new concepts of clinical pharmacy and pharmaceutical care which are quite different than the traditional practice of dispensing or marketing (medical representatives) that influenced the physician's pharmacist relations for the last decades, it will be necessary to evaluate efficacy of ward based services and how physicians will percept and interact with the new practice which is thought to be the dominant pharmacy practice in the few coming years.

The aim of this study was to introduce and evaluate ward based clinical pharmacy services (CPS) in a Respiratory Diseases (RD) clinic of Near East University Hospital in Turkish Republic of North Cyprus (TRNC) and assess its efficacy and physician's perceptions toward the services. The study was a prospective interventional study introducing CPS's and documenting it over the study period. A questionnaire investigating physicians' perceptions and attitude was also delivered to all internal medicine physicians' including RD physicians on baseline. After the end of the study physician's experience was also evaluated Interventions were recorded and later evaluated by an independent clinical committee for their feasibility and effect on patients. At the end, clinical pharmacist was recognized as an expert in the therapeutic use of medications, providing a unique set of knowledge and skills to the health care system. The introduction of CPS's with-in the healthcare team lead to clinically relevant and highly accepted optimization of medicine use in different wards and clinics including RD clinic in the case of this study, it was relatively well perceived by physicians in TRNC, but also could be more valued if more optimized and practiced by talented proactive clinical pharmacists in ward-based manner. a practice which should be generalized to all health care settings in Turkey and TRNC to achieve rational drug use.

**Key Words: Pharmacy practice, clinical pharmacy, hospital pharmacy, pharmaceutical care physicians, pharmacist, relationship, perceptions.**

## ÖZET

**Abdikarim M.abdi, Klinik Eczacılık Servislerinin Tanıtımı: Göğüs Hastalıkları Kliniğinde Etkinliği ve Kuzey Kıbrıs Türk Cumhuriyeti YDÜ Hastanesi Servisleri Hekimlerine Klinik Eczacılığı Tanıtma. Yakın Doğu Üniversitesi, Sağlık Bilimleri Enstitüsü, Klinik Eczacılık Master Tezi, Lefkoşa, 2014.**

Klinik eczacılar, ilaçla tedavide, en doğru bilginin başlıca kaynaklarındandır. Tedaviyi güvenilirlik, uygunluk ve maliyet yönünden geniş bir perspektifte inceleyen, hastanın tedaviden maksimum fayda almasını sağlamakla beraber tedavi sürecinde gerekli bilgileri de hastaya veren sağlık profesyonelleridir. Geçtiğimiz son on yılda, doktorların ve eczacıların ilişkilerinden etkilenecek, geleneksel olan eczane eczacılığından tamamen farklı olan, klinik eczacılık ve farmasotik bakım alanlarının yeni konseptleri gündeme geldi. Bu birimler, klinik servislerin etkinliğini ve hekimlerin, eczacıların bu yeni alanda onlarla iletişim ve etkileşimini değerlendirmek için gerekli olacaktır.

Kuzey Kıbrıs Türk Cumhuriyeti (KKTC) Yakın Doğu Üniversitesi Hastanesi Göğüs Hastalıkları (GH) Kliniklerinde yapılan çalışmanın amacı; kliniklerdeki, klinik eczacılık servislerini tanıtmak, değerlendirmek ve hekimlerin bu servise bakış açılarını belirlemektir.

Çalışma 2013 Aralık ayı başından 2014 Şubat ayı başına kadar Göğüs Hastalıkları kliniklerinde yapılmıştır. Başta GH kliniği olmak üzere iç hastalıklar kliniklerindeki hekimlerin klinik eczacılara olan bakış açıları ve tutumları anket yöntemiyle incelenmiştir. Çalışmanın sonunda hekimlerin deneyimleri değerlendirildi, klinik eczacı olarak yapılan müdahaleler kaydedildi ve bağımsız bir klinik komite tarafından hastalar üzerinde ki etkisinin uygunluğu değerlendirilmiştir.

Klinik eczacı, ilaçların teröpatik kullanımında, sağladığı bilgi ve beceriler ile sağlık sistemine faydalı eleman olarak hizmet üretir. Klinik eczacılık uygulamalarını sağlık ekibine dahil etmek, göğüs hastalıkları kliniğinde olduğu gibi, diğer kliniklerde de önemli ölçüde ilaç kullanımının en iyi şekilde gelişmesine olanak sağlayacaktır, bu çalışma KKTC'deki hekimler tarafından çok olumlu karşılanmıştır ve tabi ki bu konuda daha iyi eğitim almış ve klinik çalışmalarda yetenekli olan, aktif eczacıların katılımlarıyla klinik eczacılık daha iyi bir noktaya gelecektir. Klinik eczacılık çalışmaları Türkiye ve KKTC'de sağlık sistemine dahil edilirse akılcı ilaç kullanımı daha da yaygınlaşacak ve başarılı olacaktır.

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## **LIST OF ABBREVIATIONS:**

ACS: acute coronary syndrome.  
ACCP: American College of Clinical Pharmacy  
ACEI: ANGIOTENSIN CONVERTING ENZYM INHIBITORS  
AHA: AMERICAAN HEART ASSOCIATION  
APA: American pharmacists association  
ASHAP: The American Society of Health-System Pharmacists  
A1C: Glycated hemoglobin  
CHD: chronic heart disease  
COPD: chronic obstructive pulmonary disease  
CVD: cardiovascular disease  
CP: clinical pharmacist  
CPS: clinical pharmacy services  
DM: diabetes disease  
DTP: drug-therapy problem  
FDA: food and drug administration  
IFP: International Pharmaceutical Federation  
MI: Myocardial Infarction  
MTM: medication therapy managment  
NEU: Near East University  
PEV: peek expiratory volume  
RD: respiratory diseases  
SD: standard deviation  
TRNC: Turkish Republic of North Cyprus.  
WHO: world health organization

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# 1. Introduction

***“Pharmacists should move from behind the counter and start serving the public by providing care instead of pills only. There is no future in the mere act of dispensing. That activity can and will be taken over by the internet, machines, and/or hardly trained technicians. The fact that pharmacists have an academic training and act as health care professionals puts a burden upon them to better serve the community than they currently do.”***

(From: Pharmaceutical care, European developments in concepts, implementation, and research: a review.)

For centuries, the profession of pharmacy has provided services of fundamental value to society. But since the industrial development this services retarded much restricting only to dispensary and distribution of medicines. Rather than restricting the pharmacist’s professional role to merely supplying and dispensing drugs, in a 1989 paper, Hepler and Strand first reached this introductory conclusion under the title “Opportunities and Responsibilities in Pharmaceutical Care,” they proposed a revolutionary philosophy of pharmacy practice that went far beyond the expectations of most pharmacy practitioners, going far beyond the term “clinical pharmacy” to a more responsible approach of pharmaceutical care.

They reviewed the alarming extent of drug-related morbidity and mortality and thus reached the conclusion that this problem could only be resolved by a dramatic change in the pharmacist’s professional function. A change affecting practice in hospitals, community pharmacies, and of course pharmacy education, stressing that the practice of pharmacy “must restore what has been missing for years: a clear emphasis on the patient’s welfare, a patient advocacy role with a clear ethical mandate to protect the patient from the harmful effects of ‘drug mis-adventuring’” [1,2].

In recent years as medication use continues to grow, and therapeutically regimens become more complex, our health care systems have become more prone to medication errors and adverse drug events. Clinical pharmacists provide pharmaceutical care and Medication Therapy Management services which have been shown to help reduce medication errors, adverse drug events, and costs. Such services are no more regarded as optional and should be integrated in every health care system [3].

Pharmaceutical care the clinical pharmacist major role is now understood as the “a process in which a pharmacist cooperates with a patient and other health professionals in designing, implementing, and monitoring a therapeutic plan that will produce specific therapeutic outcomes for the patient.” pharmacists' compromise to obtain the maximum benefit from the pharmacological treatments of the patients , and since the concept started at USA before around 26 years ago it became now one of the most critical roles thousands of pharmacists do all around the world , and much of the benefits of this practice is recently well documented and assessed by clinicians in compare to possible costs for this practice on health care institutions, especially for common pathologies such as diabetes, hypertension, asthma, hyperlipidemia, chronic pain, rheumatic diseases or psychiatric disorders, as well as in poly-medicated patients. [4]

In the transition to this new more secure health system, it will be obvious that the collaboration between healthcare team members is crucial for the success of the care process which can be studied and expected by carrying perception and experience studies which show how different healthcare members see and cooperate with other members specially the pharmacist in our case.

In this study we introduce clinical pharmacy services (CPS) to a respiratory clinic in an educational hospital at Northern Cyprus, and then we evaluate these services both in terms of quantity and quality.

Also we study physician's perceptions to CPS's and the roles and duties of the clinical pharmacist, and their experience after the introduction of these services in a respiratory clinic.

This study is the first of its kind in Cyprus, and it's supposed to be of much value for pharmacy faculties in implementing clinical pharmacy education and practice in hospitals in Cyprus, which they started to work on.

In the following sections, we review the recent shift in pharmacy practice, current definition and responsibilities of clinical pharmacists, there effect in different clinical settings and how physicians in different countries perceive pharmaceutical care before presenting our study findings.

Section one will summarize the major shifts in pharmacy practice during the 20th century, it will also address one of the major reasons for this shift which the concern of rational drug use, section two is discussing clinical pharmacy and pharmaceutical care definition and duties as

viewed by different pharmaceutical bodies and organizations, it also explains what is meant by medication therapy managements and its core elements as the most advanced pharmaceutical care tool.

Section three will mention the effect of clinical pharmacy both from economical and clinical viewpoints, while section four address the importance of physician's perceptions toward the new pharmacist role and their current experience with pharmacists carrying pharmaceutical care.

The second part of this thesis contains sections five to eight which are about our study, its aims, objectives, methodology and results, which at end are summed up with a brief conclusion.

## **1.1 Pharmacy Practice Development**

Over the past half century, pharmacy practice has shifted away from being just product or medicine focused to more focus on patient care. This move started many years after the development of large pharmaceutical industries and their stores during the first half of the twentieth century and by this, pharmacists gradually lost three quarters of their professional function, that had characterized the work of pharmacists for nearly one thousand years; compounding, procuring and storing of medicinal products [5].

Pharmacists then after concentrated on the remaining professional function, mainly dispensing and distributing medicine till the mid 1960's just after developing the term of clinical pharmacist and starting the focus upon assuring safe, effective, and cost-efficient therapeutic outcomes for patients. This led to an initiate of a sharp criticism between pharmacy practitioners about the role and practice of pharmacy at that time [6].

Pharmacists found themselves becoming too commercialized and lost much of their professionalism in the presence of a vacancy and a crucial role for them to practice their deep pharmacotherapy knowledge in face of increasing complexity of drug regimens with dramatic increase in the number of medicines in the market which led to emergence of a worldwide concern and need for controlling the quality and the rational use of medicines [7-9].

Here pharmacists established their practice in clinical consultations in hospitals with the availability and easier access to clinical data and other patient information in modern hospitals and forced by challenging inter-professional practice settings in the mid 1970's [10,11].

This practice was widened and more developed in the following years increasing the services introduced by pharmacist along with the societal need for both the distributive and the more highly specialized professional services provided by pharmacists which has been also well documented.

Since after, pharmacy practice continued to grow from clinical pharmacy where only consultations are given to medication therapy management. In an effort to improve clinical outcomes and manage costs for those with chronic conditions, managed care organizations

developed also disease state management programs [12]. Finally Pharmaceutical care originated in the 1990's as the practice where the practitioner (pharmacist) takes responsibility for a patient's drug related needs and is held accountable for this commitment. These developments which mainly took place first in the USA and thus the American pharmacists have much of its credit were later on generalized and practiced world widely in majority of the developed countries [13,14].

In United Kingdom and Europe a slower development in pharmacy practice than USA is noted with a lot of variations between hospitals in type of clinical pharmacy services offered from almost 100% of hospitals having pharmacists who monitored drug therapy to less than 10% for services such as infection control, clinical audit or medical staff education, which is clearly due to the absence of specific directions from the governments and from the pharmacy professional bodies [15,16].

The practice of clinical pharmacy in UK started from hospital pharmacists who were mostly engaged in traditional pharmaceutical activities such as dispensing and manufacturing. Then, due to increasing range and sophistication of medicines available, awareness of medication errors and the widespread use of ward-based prescription charts brought pharmacists out of the dispensary and on to the wards in increasing numbers [17].

This was initially described as 'ward pharmacy' and was mostly a post hoc process with the emphasis on the safe and timely supply of medicines in response to medical and nursing demands. However, the service quickly evolved into something significantly more proactive, seeing pharmacists interacting with patients and other healthcare professionals and directly intervening in the patient care process [18]. The growth in these services over the 1970s and 1980s was said to represent a change in hospital pharmacy from product orientation to patient orientation and was formally acknowledged as 'clinical pharmacy' in the 1986 Nuffield report [19]. The report welcomed these changes and recommended an increased role for hospital pharmacists through the development of clinical pharmacy services.



As clinical pharmacy services expanded, there was increasing specialization, with the expertise of individual pharmacists in certain therapeutic areas contributing to more significant developments in service provision, these services were continually expanding with more reports and white papers beside efficacy studies declaring roles and services and acknowledging clinical pharmacy role in ensuring patient safety and appropriate use of medicines, as a service proofed to be cost-effective.

This led finally the Department of Health to recognize pharmacists' clinical skills and expertise as an integral part of delivering better services to patients in the 2008 pharmacy White Paper, and reinforced this in 2010, identifying their role in optimizing the use of medicines [20-22].

Pharmaceutical care, the ground-breaking concept in the practice of pharmacy which emerged first in the USA by Hepler and Strand, was early adopted in Europe and UK and widely accepted [23]. In 1998, a Statement of Professional Standards in Pharmaceutical Care was adopted by the International Pharmaceutical Federation (FIP). It provides guidance to pharmacists and national health care organizations as they begin to implement broad pharmaceutical services in their countries. FIP supports the concept of pharmaceutical care but recognizes the individual needs of different countries [24].

Nowadays, though clinical pharmacy and pharmaceutical care have become the dominant form of practice for thousands of pharmacists around the world, with many of them specialized or sup-specialized in the different areas of medical practice e.g. Cardiology and infectious diseases, oncology, nephrology or pediatrics. In many American states, clinical pharmacists are given prescriptive authority under protocol with a medical provider (i.e., MD or DO), and their scope of practice is constantly evolving. In the United Kingdom clinical pharmacists are given independent prescriptive authority.

But yet many challenges and implementation barriers exist, which are attributable to problems in education, skills, resources and environment [25,26].

First the practice of pharmaceutical care is new, in contrast to what pharmacists have been doing for years, and because pharmacists often fail to assume responsibility for this care, they

may not adequately document, monitor and review the care given [26]. Accepting such responsibility is essential to the practice of pharmaceutical care.

Though the knowledge base of pharmacy graduates is changing, as these graduates move into practice, so pharmacy practice itself will change, to reflect the new knowledge base, still many universities and pharmacy schools adopt different curriculums, while many not attaining minimum requirements for future pharmacists to carry their new crucial role. Others don't have capabilities of experienced teachers or not receiving enough clinical training or are with weak pharmacotherapy background which does not qualify them to assume the new challenges in clinics [26-28].

Also, pharmacists already in practice in pharmacies both hospitals based and community were mostly educated on the basis of the old practice, focused on pharmaceutical product. If these pharmacists are to contribute effectively to the new patient-centered pharmaceutical practice, they must have to acquire the new knowledge and skills required for their new role. So they must become life-long learners, which a new responsibility and role new pharmacist must offer.

Also many countries need much more developments in their health legislations, many more institutions has misperceptions about clinical pharmacists and thus lead to weak communication and failure of pharmaceutical care which shall be provided by pharmacists, if it's even allowed to be practiced at all .

All these, need much more collaborative efforts from international pharmaceutical organizations and boards to clear and unify minimum needed requirements for pharmacy graduates and also to push toward the adoption of recent definitions and practice services of pharmaceutical care using the huge body of literature currently available which justifies cost effectiveness and need to pharmaceutical care which no more is considered to be an optional measure [28-30].

## 1.2 RATIONAL DRUG USE: Is It Compulsory?!

Rational drug use require “*patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community*” [31].

So the main points that must be met to ensure rational drug therapy are:

1. Right patient,
2. Right diagnosis,
3. Appropriate dose,
4. Appropriate dosage form,
5. Appropriate route of administration,
6. Appropriate frequency of administration,
7. Appropriate duration of treatment,
8. Appropriate information to the patient,
9. Adequate follow up.

Or simply means "prescribing right drug, in adequate dose for the sufficient duration and appropriate to the clinical needs of the patient at lowest cost"[32,33].

Lack of information, poor communication between health professional and patient, lack of diagnostic facilities/Uncertainty of diagnosis, increasing demand from patients to more medications, defective drug supply system and ineffective drug regulation plus promotional activities of pharmaceutical industries, all are reasons for irrational use of drugs which lead to:-

1. Ineffective and unsafe treatment
2. Exacerbation or prolongation of illness.
3. Distress and harm to patient
4. Increase the cost of treatment

In order to implement rational drug use we have first to measure the irrationality in our use to medicines from multiple points, such as:

1. The types of irrational use of medicines.
2. The amount of irrational use.
3. The reasons why medicines are used irrationally.

In the second International Conference on Improving the Use of Medicines (ICIUM) that took place in Thailand in 2004 three major recommendations were made:

1. Countries should implement national programs in order to improve the use of medications and these programs should:
  - a) Be long-term;
  - b) cover all levels of health care in public and private sectors;
  - c) be based on local evidence from inbuilt monitoring system;
  - d) separate prescribing and dispensing functions;
  - e) extend broad-based insurance coverage;
  - f) measure drug prices which influence access to medicines;
  - g) avoid flat patient visit fees which encourage polypharmacy;
  - h) Encourage generic prescribing and dispensing policies provided there are drug quality assurance programs.
2. Successful interventions should be scaled up and their impact regularly monitored e.g.
  - a) Prescription of 3-day antibiotic therapy for pneumonia which is just as effective as 5 days;
  - b) Use of multi-faceted coordinated interventions which are more effective than single ones;
  - c) Implementation of structured quality- improvement processes possibly through Drug and Therapeutic Committees.
3. Interventions should address community medicines use by:
  - a) improving patient adherence as an integral part of global treatment programs;
  - b) encouraging school programs that teach about how to use medicines;
  - c) regulating pharmaceutical promotion (much of which continues to be excessive and inappropriate in many low and middle income countries);
  - d) Evaluating medicines use in chronic diseases and how to promote more cost-effective long-term use.[30]

However, rational use of medicines keeps an exception not the rule, when we say people who do receive drugs, more than half of all prescriptions are incorrect while more than fifty percent of the people involved use medicines incorrectly worldwide according to WHO reports [34].

In addition, there is a growing concern at the increase in the global spread of antimicrobial resistance, a major public health problem. World health organization reports reveal that findings of up to ninety percent resistance to original first-line antibiotics such as ampicillin and co-trimazole for shigellosis, where else up to seventy percent resistance to penicillin is seen for bacterial meningitis and pneumonia, also up to ninety eight percent resistance to penicillin for gonorrhea, and seventy percent resistance to both cephalosporins and penicillins for nosocomial *Staph.Aureus* infections. [35]

For this the FIP statement in 2000 declared among other recommendations to combat AB resistance, the readiness of pharmacists to collaborate with physicians and other healthcare providers in an effort to overcome AB resistance and increase public awareness to the correct use of antibiotics .[36]

Hence the mission of the pharmacy profession must address the needs of society and individual patients. At one time, the acts of deciding on drug therapy and implementing it were relatively simple, safe and inexpensive. Physicians prescribed and the pharmacists dispensed. However, there is substantial evidence to show that the traditional method of prescribing and dispensing medication is no longer appropriate to ensure safety, effectiveness and adherence to drug therapy [36].

The consequences of medicine-related errors are costly in terms of hospitalizations, physician visits, laboratory tests and remedial therapy. In developed countries, 4%-10% of all hospital inpatients experience an adverse drug reaction – mainly due to the use of multiple drug therapy, especially in the elderly and patients with chronic diseases. In USA, for example, it is the 4th–6th leading cause of death and is estimated to cost up to US\$130 billion a year. Elsewhere, in UK it accounted for £466 million (over US\$812 million) in 2004 [37].

Another concern is also the access to medicines of assured quality which also remains a major concern. One third of the world's population does not yet have regular access to essential medicines. For many people, the affordability of medicines is a major constraint [38]. Those

hardest hit are patients in developing and transitional economies, where 50%–90% of medicines purchased are paid for out-of-pocket. The burden falls most heavily on the poor, who are not adequately protected either by current policies or by health insurance [38,39].

The logistical aspect of distribution – often seen as the pharmacist’s traditional role, especially in health institutions – represents another challenge. Moreover, in many developing countries 10%–20% of sampled medicines fail quality control tests [40].

While appropriate drug therapy is safer and more cost-effective than other treatment alternatives, there is no doubt that the personal and economic consequences of inappropriate drug therapy are enormous. It is important for society to be assured that spending on pharmaceuticals represents good value for money. In view of their extensive academic background and their traditional role in preparing and providing medicines and informing patients about their use, pharmacists are well positioned to assume responsibility for the management of drug therapy [41].

In conclusion because drugs are inherently dangerous substances and the pharmacists’ knowledge about their proper preparation, storage, and handling is greater than that of any other professional group, adding this to the alarming numbers of drugs caused mortality and morbidity, pharmacists began to develop a more technologically advanced role in quality assurance and also patient care as pharmaceutical care and clinical pharmacy to hold up their responsibilities [14, 30, 42].

## **2. Clinical Pharmacy: Definition & Duties of Pharmaceutical Care and Medication Therapy Management (MTM) Services.**

### **2.1 What's clinical pharmacy?**

Clinical pharmacy is defined as the area of practice in which pharmacists provide patient care that optimizes medication therapy and promotes health; wellness and disease prevention.[43] though their movement initially started within hospitals and clinics, Clinical pharmacists care for patients in all healthcare settings, they often collaborate with physicians and other healthcare professionals.

This practice of clinical pharmacy embraces the concepts of pharmaceutical care, rationalizing drug therapy and use, medicines management or medicine therapy management (MTM), the last encompasses the entire way in which medicines are selected, procured, delivered, prescribed, administered and reviewed so to optimize the contribution that medicines make to achieve the desired outcomes of patient care. [44]

The American pharmacist association (APA ) also used the definition of clinical pharmacy as "The area of pharmacy concerned with the science and practice of rational medication use".

This declares the role of clinical pharmacists as to rationalize drug used in the different health settings and areas of practice. This embraces the philosophy of pharmaceutical care that blends a caring orientation with specialized therapeutic knowledge, experience, and judgment for the purpose of ensuring optimal patient outcomes.

Clinical pharmacists possess in-depth knowledge of medications added to a foundational understanding of the biomedical, pharmaceutical, socio-behavioral, and clinical sciences. Together with this they aim to achieve desired therapeutic goals, by applying evidence-based therapeutic guidelines, which evolve sciences and technologies, considering relevant legal, ethical, social, cultural, economic, and professional principles.

In accordance, they assume responsibility and accountability in healthcare settings, for managing medication therapy both independently and in collaboration with other healthcare professionals.

We can organize the definition of "clinical pharmacy" into three major sections; that is the pharmacist, clinical pharmacy and the roles of the clinical pharmacist in the healthcare system. The words in the definition were carefully chosen to indicate a distinct meaning.

Clinical Pharmacy in its definition when carries these concepts as a discipline of "optimizing therapy and promoting health, wellness, and disease prevention" essentially highlights to the focus on both pharmacologic and non-pharmacologic strategies for promoting patient health.

It also by embracing the concept of pharmaceutical care, clearly indicate to the fact that it relies on caring values with specialized knowledge, experience, and judgment emphasizing the critical importance of having a synergy between in-depth therapeutic knowledge, clinical experience, caring ethos, and expert judgment.

Engaging also clinical pharmacy as a discipline in research contributes to the generation of a new knowledge that improves human health and life's quality.

The Clinical Pharmacist when Stated explicitly that he cares for patients in all health care settings underscores two major points: first that clinical pharmacists provide care to their patients (i.e., not only consultations), and that they should practice in all practice settings.

By applying evidence and evolving sciences beside the application of legal, ethical, social, cultural, and economic principles, the definition remind us that clinical pharmacy practice also takes into account societal factors which extend beyond science, and by assuming responsibility and accountability for achieving therapeutical goals the definition clears that clinical pharmacist are more than just consultants.

In stating the roles of a clinical pharmacist within the Health Care System, noting that defining the clinical pharmacist as an expert in the therapeutic use of medications indicates that; they are recognized as providing a unique set of knowledge and skills to the health care system and thus therefore qualified to assume the role of drug therapy expert. This should be used to ensure and advance rational drug therapy, thereby averting many of the medication therapy misadventures that arise following inappropriate therapeutic decisions. While stating that CP's are a primary source of scientifically valid information and advice on the best use of medications declares that they serve as an objective, evidence-based source of therapeutic



information and recommendations, and as an expertise, that extends beyond traditional medications, to include nontraditional therapies as well.

Finally, saying that clinical pharmacists routinely provide therapeutic evaluations and recommendations emphasize the fact that their daily practice involves constant consultation to patients and healthcare professionals regarding medication therapy evaluations and recommendations."[43]

## **2.2 Pharmaceutical Care:**

The American Society of Health-system Pharmacists (ASHP) believes that pharmaceutical care is an important new concept that represents growth in the profession beyond clinical pharmacy as often practiced and beyond other activities of pharmacists, including medication preparation and dispensing, which they consider to be also important duties that must be carried by pharmacists but also integrated with pharmaceutical care [50].

Pharmaceutical care, which is care delivered at the individual patient level, was first defined by Mikeal et al in 1975 as 'the care that a given patient requires and receives which assures safe and rational drug usage [46].

Since then there have been many changes to this definition, but the one that lays a foundation for most resources is that attributed to Hepler and Strand of pharmaceutical being the responsible "provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life" [14].

This quit different to what pharmacists used to do in term of individualizing care directly to individual patients rather than previous practice which Walker R defined as "the application of pharmaceutical knowledge, skills and resources to the science and art of preventing disease, prolonging life, promoting, protecting and improving health for all through the organized efforts of society" [45].

In 1998, the International Pharmaceutical Federation (FIP) adopted Helper's and Strand definition with one significant change which is probably a more realistic goal, especially for chronic progressive diseases, they added "improve or maintain a patient's quality of life". Becoming more suitable in patients where maintenance of quality of life would itself be a significant achievement. [24]

The keywords in this definition are "responsible provision" and "definite outcomes". Are pharmacists' ready to accept this responsibility? Are they reviewing a prescription or a patient medication record, talking to a patient or responding to symptoms? They are then automatically assessing needs, prioritizing and creating a plan to meet them. But what they often fail to do is to accept responsibility for this care which is essential to the practice of pharmaceutical care, while they do not adequately document, monitor and review the care given [47].

By the practice of pharmaceutical care, it puts on the pharmacist the responsibility of the patient for the prevention of drug-related illness.

Practicing this, the pharmacist evaluates a patient's drug-related needs, after that it must be determined whether one or more drug therapy problems exist, if present, pharmacists should work with the patient and other healthcare professionals to design, implement and monitor a care plan, a plan that must be kept as simple as possible, and maybe referenced to relevant evidence-based guidelines [48].

The care plan aims to resolve the actual DTP's and prevent potential ones becoming a reality.

A DTP (drug therapy problem) is known as an undesirable event, which a patient experience and that involve, or is suspected to involve drug therapy, which actually or potentially interferes with a desired patient outcome [49].

Pharmaceutical care should be provided ideally to all patients receiving pharmacy services, though, due to limited resources, this is not always possible while pharmacists should prioritize particular patients in such situations.

Substantial inconsistency in the description of the concept of pharmaceutical care yet exists. Many consider it as a new name for clinical pharmacy; others have described it as anything that may lead to beneficial results for patients which is introduced by the pharmacist. [47].

The principal elements of pharmaceutical care are that first, it is medication related, and thus care involves not only medication therapy (the actual provision of medication) but also decisions about medication use for individual patients. This shall include decisions not to use medication therapy as well as judgments about medication selection, dosages, routes and methods of administration, medication therapy monitoring, and the provision of medication-related information and counseling to individual patients.

Secondly it's a care that is directly provided to the patient, which caring is central for it, i.e. a personal concern for the well-being-ness of the patients, which ultimately must be a one-to-one relationship between a caregiver and a patient. The pharmacist cooperates directly with other professionals and the patient in designing, implementing, and monitoring a therapeutic plan intended to produce definite therapeutic outcomes that improve the patient's quality of life.

The third key is outcomes; also pharmaceutical care provides definite outcomes, It is the goal of pharmaceutical care to improve an individual patient's quality of life through achievement of definite (predefined), medication-related therapeutic outcomes which are either, cure of a patient's disease, or elimination or reduction of a patient's symptomatology, arresting or slowing of a disease process or preventing a disease or symptomatology.

Outcomes are intended to improve the patient's quality of life. Some tools exist now for assessing a patient's quality of life. These tools are still evolving, and pharmacists should maintain familiarity with the literature on this subject. [51, 52]

Responsibility acceptance is very crucial also, since beneficial exchange in which the patient grants authority to the provider and the provider gives competence and commitment to the patient is one of the fundamental relationships in any type of patient care. [50,14]

Lastly as an accountable member of the health-care team, the pharmacist must document the care provided. The pharmacist is personally accountable for patient outcomes (the quality of care) that result from the pharmacist's actions and decisions. [53-56]

### **2.3 MTM as Pharmaceutical Care Key Practice Element:**

Medication Therapy Management is a distinct service or group of services that optimize therapeutic outcomes for individual patients. As part of pharmaceutical care services they are independent of, but can occur in conjunction with, the provision of a medication product.[57]

Medication Therapy Management encompasses a broad range of professional activities and responsibilities within the licensed pharmacist's, or other qualified healthcare provider's, scope of practice. A program that provides coverage for MTM services must include:

- a. Patient-specific and individualized services or sets of services provided directly by a pharmacist to the patient. (Such services are different from formulary development and use, generalized patient education, and other population-focused quality-assurance measures for medication use).
- b. Face-to-face interaction between the patient and the pharmacist as the preferred method of delivery. When patient-specific barriers to face-to-face communication exist, patients shall have equal access to appropriate alternative delivery methods. Structures supporting patient–pharmacist relationship maintenance should be assured in MTM programs.
- c. Opportunities for pharmacists and other qualified healthcare providers to identify patients who shall receive medication therapy management services
- d. Payment for medication therapy management services consistent with contemporary provider payment rates that are based on the time, clinical intensity, and resources required to provide services.
- e. Processes to improve continuity of care, outcomes, and outcome measures. [57]

The MTM service model in pharmacy practice includes the following five core elements:

- Medication therapy review (MTR). The medication therapy review (MTR) is a systematic process of collecting patient-specific information, assessing medication therapies to identify medication-related problems, developing a prioritized list of medication-related problems, and creating a plan to resolve them. [66]

Medication related problems could be related to clinical appropriateness of a medication, dose and dosing regimen, indications, contraindications, potential adverse effects, and potential problems with concomitant medications, therapeutic duplication or other unnecessary medications, adherence to the therapy, medication cost considerations , etc. .

A plan is developed to resolve such problems, and patients are provided with education and training on the appropriate use of medications and monitoring devices, also they are coached to be empowered to manage their medications, and then monitored their response for safety and effectiveness.

- Personal medication record (PMR): This is a comprehensive record of the patient's medications (prescription and nonprescription medications, herbal products, and other dietary supplements) that is received by the patient.

Ideally, the patient's PMR would be generated electronically, and updated routinely, but it also may be produced manually, but the important thing is that the information should be written at a literacy level that is appropriate for and easily understood by the patient. PMR is best provided on discharge. It includes for each medication, the drugs names and doses, the indications, instructions for use, start and stopping dates, prescribers contact information, and special instructions. Also information of patient name, birth date phone number emergency contact information names and phones of primary care physician, pharmacy/pharmacist, allergies, other medication-related problems.

Else it's important to include potential questions for patients to ask about their medications during healthcare visits (e.g., when you are prescribed a new drug, ask your doctor or pharmacist), dates of last update to the PMR, dates of last review by the pharmacist, physician, or other healthcare professional.

- Medication-related action plan (MAP): this is a patient-centric document containing a list of actions for the patient to use in tracking progress for self-management. A care plan is the health professional's course of action for helping a patient achieves specific health goals. [70] The care plan is an important component of the documentation core element outlined but in addition to the care plan, which is developed by the pharmacist and used in the collaborative care of the patient, the patient receives an individualized MAP for use in medication self-management.

The patient MAP includes only items that the patient can act on that are within the pharmacist's scope of practice or that have been agreed to by relevant members of the healthcare team, while it should not include outstanding action items that require physician or other healthcare professional review or approval.

It's just a simple guide for the patient to track his or her progress, coupled with education; it is an essential element for incorporating the patient-centered approach into the MTM service model. The MAP reinforces a sense of patient empowerment and encourages the patient's active participation in his or her medication-adherence behavior and overall care.

- Intervention and/or referral. The pharmacist provides consultative services and intervenes to address medication-related problems; when necessary, the pharmacist refers the patient to a physician or other healthcare professional. Interventions may include collaborating with physicians or other healthcare professionals to resolve existing or potential medication-related problems or working with the patient directly. Positive impact of pharmacist interventions on outcomes related to medication-related problems has been demonstrated in numerous studies [73-75].

- Documentation and follow-up. All MTM services should be documented in a consistent manner, and a follow-up MTM visits could be scheduled based on the patient's medication-related needs, or the patient is transitioned from one care setting to another.

Proper documentation of MTM services serve several purposes including, but not limited to, facilitating communication between the pharmacist and the patient's other healthcare professionals regarding recommendations intended to resolve or monitor actual or potential medication-related problems, Improving patient care and outcomes, enhancing the continuity of patient care among providers and care settings, ensuring compliance with laws and

regulations for the maintenance of patient records, protecting against professional liability, capturing services provided for justification of billing or reimbursement, demonstrating the value of pharmacist-provided MTM services and demonstrating clinical, economic, and humanistic outcomes of MTM.

These five core elements form a framework for the delivery of MTM services in pharmacy practice. Every core element is integral to the provision of MTM; however, the sequence and delivery of the core elements may be modified to meet an individual patient's needs. In various settings MTM services has resulted in reductions in physician visits, emergency department visits, hospital days, and overall healthcare costs [58-61].

### **3. Role of Clinical Pharmacist and Effect of Pharmaceutical Care on Different Pathologies:**

#### **3.1 The role of clinical pharmacist in clinical settings:**

Clinical pharmacists as an expert in the therapeutic use of medications, provides a unique set of knowledge and skills to the health care system and is therefore qualified to assume the role of drug therapy expert and ensure rational drug therapy [77].

We can summarize the major activities and responsibilities of clinical pharmacists in prescribing drugs, administering them, documenting professional services, reviewing drug use, communicating with patients and counseling them, preventing medication errors and providing consult for physicians and other health professionals [78].

#### **3.2 Effects of pharmaceutical care applications on most common pathologies:**

Due to the continues efforts of developing a more efficient healthcare system and role of pharmacist in achieving rational drug use clinical pharmacy practice has been widely spread to cover all specialty fields of medical treatment and centers, among these are DM clinics ,Cardiology clinics, Psychiatry, Pediatrics, and family medicine .The effect of clinical pharmacy on these fields has been well studied and documented over the last ten years .here in this review we summarize the effects of pharmaceutical care applications on most common pathologies.

##### **3.2.1 Diabetes Mellitus:**

Many studies done on effect of pharmacist interventions on glycemic control in diabetes have shown an overall improvement in A1C for patients in a diverse group of settings and across multiple study designs. Studies with smaller numbers of participants and those performed in the United States generally showed greater improvements in intervention group measures of A1C. A greater effect was also noted when pharmacists were afforded prescriptive authority. Other studies suggested that pharmacist interventions can reduce long-term costs by improving glycemic control and thus diminishing future diabetes complications [79-82].



### **3.2.2 Cardiovascular diseases:**

Several studies have shown that Pharmacist-directed care or in collaboration with physicians or nurses improve the management of major CVD risk factors in outpatients [83].

Pharmacist intervention can significantly improve medication adherence and blood pressure control in patients treated with antihypertensive agents they can modify factors affecting adherence, improve adherence and reduce BP levels in patients treated with antihypertensive agents. This suggests that one effective method of improving BP control is for pharmacists to recognize inadequate hypertension knowledge and medication adherence and develop strategies that enlist the patient as a participant in the management of his/her health also this reinforces the pharmacists' role in improving the health care system, leading to superior hypertensive patient outcomes [84,85].

Other findings related to ischemic heart disease indicate that an intensified education and care of patients after ischemic stroke by dedicated pharmacists based on a concept of pharmaceutical care may maintain the Health-related quality of life of patients [86,87].

Regarding hyperlipidemia early studies claim that Attempts to lower total cholesterol levels are likely to be more successful when combined with programs that include teamwork between physicians and pharmacists [88]. New studies suggest positive impact of clinical pharmacist; total cholesterol and other parameters were sensitive to pharmacist interventions. The implementation of clinical pharmacy services in a primary care setting has resulted in better patient lipid profile outcomes [89-91].

Other studies of Pharmacist care in the treatment of patients with HF suggest that pharmacist interventions greatly reduce the risk of all-cause and HF hospitalizations.

Interventions that include some element of pharmacist care reduced the rates of both all-cause hospitalization and HF hospitalization by almost one-third. Because HF is one of the leading causes of hospitalization, these studies recommend the addition of a pharmacist to the HF team. Other studies have confirmed that a substantial proportion of HF exacerbations can be attributed to medication misadventures, highlighting the potential importance of pharmacists on the HF team.[92-94]

### **3.2.3 Osteoporosis:**

Using a systematic approach to identify patients in need of osteoporosis pharmacotherapy, a clinical pharmacist-managed intervention resulted in clinically meaningful osteoporosis treatment initiation rates.[95]

Pharmacists are in a unique position to help reduce the burden of osteoporosis by improving the identification of high-risk patients for treatment, especially those on corticosteroid therapy.

Many studies suggest that Pharmacist intervention on the use of activated vitamin D was effective and resulted in a cost saving also pharmacist identification and counseling of patients at risk for osteoporosis results in higher DXA testing and improvements in calcium intake.[96,97]

### **3.2.4 Psychiatric diseases:**

Implementing clinical pharmacists' consult recommendations in psychiatric clinics was associated with significantly greater improvement in overall severity of illness and global improvement [98]. Psycho pharmacists provide important drug-related information to patients and consultation regarding potential neuroleptic-induced adverse effects. In addition, psychopharmacists serve as consultants to other clinicians concerning the risks associated with the use of neuroleptics and participate in neuroleptic-discontinuation clinics. Morbidity associated with neuroleptic-induced tardive dyskinesia has exposed healthcare providers to legal repercussions; therefore, pharmacy intervention may aid in the reduction of legal liability [99-102].

### **3.2.5 Pediatric Medicine:**

Researches and studies have clearly shown the positive effect of presence of a person reviewing and registering the drug records on the overall drug error rate in pediatric patients. Also a pharmacist is able to perform clinically relevant interventions in a hematopoietic stem cell transplant unit, given the complexity of the pharmacotherapy.

Studies also suggest that the coordinated efforts of pharmacists' interventions during the discharge process have a positive impact on pediatric health [103-105].

### **3.2.6 Asthma and COPD**

While as many as 60% of patients do not have their asthma under good control, and many assume this is normal! [106,107] approximately 70% of patients may be using their inhalers incorrectly. In many cases, poor or incorrect technique is the root cause of patients not having success with their medication therapy [108].

In one study carried in British Columbia, two groups were compared with interventional group receiving pharmaceutical care plus usual care while control group received only usual care, patients in the enhanced care group had 75% fewer emergency room visits over those in the usual care group [109].

Other studies on effect of pharmaceutical care on asthma and COPD patients show that pharmaceutical care program increased patients' PEFs (peak expiratory flow rates) compared with usual care but provided little benefit compared with peak flow monitoring alone.

Pharmaceutical care, based mainly on improving inhalation techniques of asthma and COPD patients (which is poor) increased patient satisfaction but also increased the amount of breathing-related medical care sought. While rare studies claim that there was no significant difference between study groups and two trials reported decreases in quality of life [110-112].

### **3.2.7 Infectious diseases:**

Recent studies declare that pharmacist interventions, interacted directly with the physicians at ward level, could play an important role in optimizing antibiotic use, thus lead to the reduction in patients' length of hospital stay and health care cost [113].

A study was done by a Chinese investigator to evaluate the impact of pharmacist interventions on antibiotic use in inpatients with respiratory tract infections in a tertiary hospital in China. All inpatients diagnosed with respiratory tract infections were enrolled. Pharmacist interventions were performed on the physicians in the intervention group. The total cost of hospitalization, cost of antibiotics, length of hospital stay and the scores of 6 items of inappropriate antibiotic use (including indication, choice, dosage, dosing schedule, duration and conversion) were analyzed. The total costs of hospitalization in the intervention

group were significant lower compared to the control group as well as the cost of antibiotics, and the patients required shorter length of hospital stay [114].

Other studies, suggested that clinical pharmacist potentially has an important role in promoting and maintaining appropriate prescribing of IV antimicrobials in hospitals. Pharmacy-led introduction of antibiotic guidelines appears to result in clinically appropriate reductions in IV therapy [115]. Also other studies proved that pharmacists in ICU contributed to optimize anti MRSA therapy and reduce the medical cost [116].

## **4. Importance of perception expectations and attitude:**

### **4.1 Perceptions and Collaborative Care Process:**

Perception can be defined as a process by which individuals organize and interpret their sensory impressions in order to give meaning to their environment. Or in simple words the way in which something is regarded, understood, or interpreted, which influence the behaviors of people and thus their decision making and decisions [117,118].

The importance of perceptions, expectations and attitude has been noticed and studied for a long time due to their critical effect on interactions between team and organization members and thus affecting the outcomes [119].

Effective collaborative practice is a key principle of health service delivery in interdisciplinary teamwork which is an essential component of best practice and chronic conditions care.

The Agency for Healthcare Research and Quality concluded that for improving patient safety it often involves the coordinated efforts of multiple members of the health care team while errors never could be prevented by perfecting individual health works i.e. doctors or pharmacists which necessitates collaboration and team working approaches [120].

This value of a team-based approach to health care has well been recognized for decades in health institutions, the introduction of collaborative approach for patient care and teamwork of interdisciplinary teams had contributed to multiple positive outcomes [121]. including less length of stay and readmissions, improved patients, team satisfaction, decreased mortality and hospitalizations while In the primary care setting, physician–pharmacist collaboration on drug therapy management has been associated with enhancing medication safety and appropriate prescribing, and improving clinical outcomes in several pathologies and chronic diseases as we mentioned earlier [122 - 125].

Perceptions about the nature and value of teamwork vary among health professionals. There is often poor understanding of roles and tasks of other professionals, Positive perceptions and attitude, clearing out roles and duties will lead to realistic expectations, which

enhance communication between healthcare team members and ultimately lead to professionalism and better outcomes of patient care process [126,127].

Extensive studies are carried all over the world currently on Implications of the interactions between physicians and pharmacists, i.e. physician's perceptions toward the newly introduced practice of pharmacy, pharmaceutical care and their attitude and experience with clinical pharmacy services.

These studies are important and address gaps in health care system and education, especially with the large shift of pharmacy practice toward pharmaceutical care and clinical pharmacy and thus need to evaluate how physicians the leaders of healthcare teams, who have a critical role in the application and success of this process and whom the pharmacist will interact with mostly beside the patients, to evaluate how do they perceive and interact with this newly expanding approach of pharmaceutical care..

#### **4.2 Studies Done on Physician's Perception toward Pharmacists:**

In United States where pharmaceutical care is best practiced and taught, though Limited research still has evaluated physician attitudes toward the new advanced pharmaceutical care practice of pharmacist-provided MTM services, Studies conducted showed physician perception and attitudes toward the new advanced pharmaceutical care practice of pharmacist-provided MTM services, is perceived as a valuable resource to optimize patient care [128]. A study done in The University of Illinois Outpatient Care Center to determine healthcare professionals, including physicians, nurses, and pharmacists perception and utilization of the MTM clinic has concluded that by providing patients with in-depth education as it relates to their prescribed medications and disease states MTM clinic was perceived as a valuable resource and These identified benefits of MTM clinic lead to frequent patient referrals specifically for aid with medication adherence and disease state management [128,129] .

A study performed also by the New York City Department of Health and Mental Hygiene aiming to obtain a better understanding of the perceptions related to pharmacist-led MTM programs among primary care physicians in NY city . Key findings from the study suggest that educating physicians on MTM and the role of pharmacists in the healthcare team is crucial to building trusting relationships for collaborative patient care. Also attaining

effective collaboration, pharmacist competency, workload and integration of documentation systems where the major concerns among physicians that the study reported (130).

Many studies reported perceptions about other clinical pharmacy services; one was to classify pharmacist-physician encounters in a family medicine center into three progressive levels of service in order to determine the physician's perception of the relative value of each level. The three levels of services were drug information, pharmacy consultation individualized to the patient, and pharmaceutical care-consultation with follow-up to monitor patient outcome. Physicians received a questionnaire with each encounter and were asked to rank questions regarding the quality of the information provided, the impact they perceived that the information had on patient care, and to assign a monetary value for each encounter. The study concluded that the physicians' perceptions toward the quality, impact, and value of pharmacy services were favorable overall, but they perceived a significantly higher quality, impact, and value to pharmaceutical care encounters than for drug information and pharmacy consultation [131].

A review done for 19 studies on clinical pharmacy services in the care of solid organ transplant patients reported Positive perceptions of patients and health care professionals with a very high rate of acceptance of pharmacist's interventions (95%), and appreciation of the services given . Services provided included beside patient education and counseling, identifying, resolving and preventing drug-related problems, and therapeutic drug monitoring [132].

Though also a study carried in Connecticut USA examining perceptions of both customers and payers beside physicians for MTM services showed that most consumers viewed pharmacists in traditional dispensing roles and were unaware of the direct patient care responsibilities of pharmacists as part of community-based health teams. Physicians noted several chronic disease states where clinically-trained pharmacists could collaborate as health care team members yet had uncertainties about integrating pharmacists into their practice workflow and payment sources for pharmacist services. The study recommends the need for disseminate the existing body of evidence on pharmacists as care providers of medication management services and the related impact on clinical outcomes, patient safety, and cost savings to external audiences [133].

Studies done elsewhere around the world show also positive perceptions for different clinical pharmacy services with many challenges also mentioned.

A French study aimed at reporting physician's expectations towards pharmacy services and their judgment on the usefulness of routine pharmacist interventions showed reduced accepted pharmacist's input in terms of drug choice or monitoring.

Young prescribers showed more positive perceptions towards clinical pharmacy. Quarter of the respondents cite the pharmacist as an active member in managing different key-points of the prescription. After being showed clinical examples from the same working place of pharmacist interventions, 73% of the prescribers consider pharmacists' interventions as useful [134].

Other researchers found that physicians and nurses valued contributions from pharmacists with regard to pharmaceutical skills, and felt that this raised awareness on prescribing quality and in all valued the pharmacists' services and reported that this collaboration improved patients' drug therapy [135].

A study conducted in china aimed at exploring physicians' perceptions and overall attitudes toward clinical pharmacy services in China, to determine the dimensions of factors underlying the physicians' perceptions of different types of services, and to analyze the determinants of physicians' overall attitudes. The study resulted in physicians having generally a positive overall attitude. Four factors seemed to influence them which are clinical pharmacists' support of physicians' decisions; auxiliary work; prescribing; and independent decision-making activities. The results showed that the degree of comfort with clinical pharmacists' support of physicians' decisions had the greatest influence on physicians' overall attitudes toward clinical pharmacy services [136].

While in Jordan a study investigating physicians' perceptions, expectations, and their actual experiences with pharmacists in hospital settings in Jordan in 2008 before the expansion of clinical pharmacy practice in Jordanian hospitals, the study was covering more than 200 physicians and concluded that Physicians in hospitals in Jordan were more likely to accept or recognize traditional pharmacy services than newer clinical services. The study recommended that increasing physician awareness of these clinical pharmacy skills will be an important step in developing a collaborative working relationship [137].

In Qatar also researchers found that physicians had low comfort and expectations of patient-oriented pharmacist roles but were not threatened to learn more about these capabilities or explore enhanced collaboration in patient care [138].



## **5. The Study Objectives, Aims, Rational, and Design**

### **5.1 Objectives Aims and Rationale:**

Clinical pharmacists are a primary source of scientifically valid information and advice regarding the safe, appropriate, and cost-effective use of medications having wide scope in drug Information and utilization, evaluation and selection medication therapy management and finally disease State Management, this made clinical pharmacists to have a wide efficient practice in many specialties in implementing rational drug use and optimizing the use of medications.

After the introduction of the new concept of clinical pharmacy and pharmaceutical care which is quite different than the traditional practice of dispensing or marketing (medical representatives) that influenced the physician's pharmacist relations for the last decades, it will be necessary to evaluate how physicians will percept and interact with the new practice which is thought to be the dominant pharmacy practice in the few coming years.

Studies on the activities of the clinical pharmacist in different wards in Turkey and Turkish Republic of North Cyprus (TRNC) are though not well established , however All leading pharmacy faculties in Cyprus started adopting clinical pharmacy based disciplines at both master and undergraduate degree (Pharm.D) levels. faculties in Cyprus are working currently in developing and implementing clinical pharmacy services in hospitals and clinics and thus studies are needed to proof efficacy in terms of utilizing drug use in hospitals and cost effectiveness of treatment process it's also essential to study physicians perceptions towards such services before widening this practice, which could lead to more rational drug use in hospitals and wards in Cyprus.

However, the implementation of clinical pharmacy services is yet very rare and limited if exists. To our knowledge, at the time this paper was prepared, the clinical pharmacy services introduced by master students at Near East University Hospital, was the only established clinical pharmacy practice all over Cyprus. The aim of this study is to introduce and evaluate ward based clinical pharmacy services in a respiratory diseases clinic of Near East University Hospital in TRNC and assess its efficacy and physicians perceptions toward the service.

No previous studies also were conducted in Cyprus describing the physician pharmacist relationship. There is a general impression that physicians do not regard pharmacists highly and do not expect them to provide any clinical services. This may be clear by the fact that none of the hospitals in the north of Cyprus have clinical pharmacies or even enough numbers of hospital pharmacists while in some settings technicians practice the dispensary duties of a pharmacist.

As such, one of the goals of this study was also to pilot whether there is a resistance from physicians to the development in pharmacists' role to a direct care giver, and to identify the nature of the relationship between physicians and pharmacists, especially those in hospitals and what will they expect from their new practice, though the number of surveyed physicians is not enough to generalize a role and thus further multicenter studies on both physicians and pharmacists perceptions attitude and experience are needed to provide a more comprehensive picture.

## **5.2 Materials and Methods**

### **5.2.1 Subjects and setting:**

The Study was carried out in the respiratory clinic from 01 January 2013, to 30 February, 2014 at Near East University Hospital, the largest and one of the leading medical facilities in Nicosia, Cyprus. It offers extensive medical services with its highly experienced specialist staff to patients from all over the world. The Hospital of Near East University has a 56,000 square-meter closed area comprising 209 private, single patient rooms, 8 operating theatres, 30-bed Intensive Care Unit, 17-bed Neonatal Intensive Care Unit and more than 30 different clinics and departments. The study is carried in the respiratory and allergic diseases clinic one of the most leading clinics in the hospital.

All inpatients covered by the respiratory clinic physicians were included whether at the intensive care or normal ward patients, three physicians' two consultants and a senior resident were in charge of the clinic patients.

### **5.2.2 Study Design:**

The Study is a prospective interventional study where pharmaceutical care services are provided by a clinical pharmacist for inpatients and documented over a period of two months. A questionnaire composed of 4 parts investigating physicians' expectations, previous experiences, and perceptions of clinical pharmacists was also delivered to all internal medicine physicians' including respiratory diseases clinic physicians on baseline. The Clinical services that were introduced by the pharmacist and documented as positive interventions and later on presented in the study included:

- 1- Participation in rounds with physicians and giving suggestions regarding therapy and acute management.
- 2- Covering each inpatient case for the RD department physicians insuring proper dosing, managing drug –drug interactions, insuring proper drugs indication and use, proper administration, prescription writing, and avoiding and detecting adverse effects caused by drugs.

- 3- Counseling patients of correct use of medications with either verbal or written materials.
- 4- Providing in-services (short lectures, presentations, etc.) for physicians or health team regarding specific topics of therapy or medications use.
- 5- Providing Drug information services (DI service) were the RD clinic physicians could ask about any information related to drugs and therapy and are provided by the clinical pharmacist in printed form from reliable mentioned resources.
- 6- Preparing printed posters and brochures on drug use on request, by the clinic physicians.

After the end of the 60 days period, a survey is also carrier to only respiratory clinic physicians to evaluate their experience and perception of the clinical pharmacy services conducted at their clinic (and also to two pediatric physicians who were clinical pharmacy services were also introduced to their clinic before the study) and were compared to the previous results obtained from baseline conducted questionnaire.

### **5.2.3 Data collection:**

Any services or interventions regarding the optimization of rational drug use were documented and registered in a work sheet along with the involved patient information and current clinical status.

Specially designed forms were filled for each patient, collecting information of patient age; complain, medical history, family history, medications use history, current medical problems, labs taken during their hospital stay and medications given during their hospital stay and on discharge.

Regarding the questionnaire, this was a self-administered questionnaire, and was delivered by hand to a sample of 17 physicians. It was composed of four parts, the first collected general demographic information about the physicians their area of practice and experience level, also there educational background and country from which their degrees were obtained from. Also there frequency of interaction and if they had any previous experience with clinical pharmacist or any contact with pharmacists in general and type or reason for such a contact were asked .

The second part of the questionnaire addressed the physicians' degree of comfort with clinical pharmacists providing clinical services, such as patient education, involvement in designing therapeutic plans for their patients or suggesting the use of nonprescription medications, monitoring outcomes of drug therapy and others.

The third component emphasized physicians' expectations of pharmacists' professional role, while the fourth part addressed physicians experience with the introduced clinical pharmacy services and was only delivered after the end of the study for physicians in the respiratory clinic and pediatricians who had previous experience with clinical pharmacy in NEU hospital before the start of this study so to have a statistically valid number of respondents (appendix I).

The used questionnaire was obtained from previous studies done to evaluate physician's perceptions and experience. It was developed by researchers who conducted a study in 2004 and distributed the questionnaire to physicians in Kuwait Modifications suitable to Cyprus medical institution were made to the original questionnaire.

#### **5.2.5 Data analysis and validation:**

Statistical analysis was done by an independent statistician also relevance and significance of each intervention and service were evaluated by an independent committee using a standardized method for characterizing drug therapy related problems and services (appendix II).

Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 15) software. Data were described using frequency distribution. Chi-square tests were used for some comparisons.

#### **5.2.5 Ethical Considerations:**

Confidentiality was assured during the study and also patient's privacy, a Letter of ethical clearance was obtained from the Institutional Review Board (IRB) of Near East University Hospital. Only Initials were used during the study and other information of address and occupation were not recorded during the pharmaceutical care. Also health and economical outcomes were insured for patients since DTP's were identified and resolved during the study and the pharmaceutical care given (appendix III)

## 6. Results:

Fourteen physicians responded to the baseline survey from the 17 who received it (82.35%). The median age was middle aged between 36 and 46 years old, more than half were men (57%). Mainly being Turkey mainlanders (50%) or Cypriot (35.7%) where only few were from Europe (7.1%) or Middle East (7.1%). Four of each five physicians (78.6%) obtained their degree and medical practice from Turkey while one physician obtained his degree from Cyprus, and two physicians are graduates of east and Western Europe respectively, as shown in **Table 1**.

**Table 1. Personal information of respondents n = 14**

The variable	n (%)
Age	
Less than 35 yrs.	28.6%
36-46 yrs.	42.9%
More than 47 yrs.	28.6%
Median age group	36-46
Gender	
Male	57.1%
Female	42.9%
Nationality	
Cypriot	35.7%
Turkish mainlander	50%
Others	14.3%
Country where medical qualification was obtained	
Cyprus	7.1%
Turkey	78.6%
Western Europe	7.1%
Eastern Europe "included Russia"	7.1%
Current position	
Trainee	0
Junior	7.1%
Senior	14.3%
Fellows	14.3%
Consultant	64.3%
Current area of practice	
Internal Medicine	85.7%
Pediatrics	14.3%

All of the physicians work currently in Near East University Hospital, they include 9 consultants (64.3%), two fellows, two senior physicians and one junior, all practicing in internal medicine science sub-divisions except two (14.3%) pediatric physicians.

None of the physicians (92.9%) had a previous interaction or rarely had with pharmacists except one physician, also majority (86.7%) never worked with a clinical pharmacist before, while main reasons for interaction if ever occurred were: for drug interaction queries (28.6%), or side effects queries (21.4%), while few physicians reported drug alternatives (14.3%) drug availability (14.3%) or others (21.4%) to be the common reasons for interaction (**Table 2.**).

**Table 2. Frequency and reasons of interactions between physicians and pharmacists (n =14)**

<b>Frequency of interactions</b>	<b>n (%)</b>
Never/rarely	92.9
Once a week	7.1
Once a day/more	
<b>ever worked with a clinical pharmacist</b>	
Never	86.7%
Yes, I did work before	14.3%
<b>Reasons for interaction</b>	
Drug-availability queries	14.3%
Side-effects queries	21.4%
Drug-alternative queries	14.3%
Drug-dosage queries	0
Drug-interaction queries	28.6%
Others	21.4%

When asked to assess their comfort with specific duties of pharmaceutical care, physicians claimed to be most comfortable with activities such as monitoring outcomes of pharmacotherapeutic regimens (64.3% comfortable, 21.8 % moderately comfortable) involving in designing and monitoring pharmacotherapeutic regimens, detecting and preventing prescription errors (64.3% comfortable, 21.8 % moderately comfortable) and providing patient education (57.1% comfortable, 28.6 % moderately comfortable) respectively (**Table 3**).

While physicians seemed uncomfortable with activities such as suggesting use of nonprescription medications (42.9% uncomfortable, 35.7 % moderately comfortable) suggesting use of prescription medications to patients like antibiotics (50% uncomfortable, 28.6 % moderately comfortable) and even treating minor illnesses like headaches (50% uncomfortable, 28.6 % moderately comfortable) though they seemed neutral for pharmacist suggesting use of prescription medications to physicians (42.9% moderately comfortable, 28.6 % comfortable 28.6% uncomfortable ).

**Table 3. Physicians’ degree of comfort with pharmacists providing different pharmaceutical care services n=14.**

<b>Pharmacists’ duty</b>	<b>Comfortable (%)</b>	<b>Moderately comfortable (%)</b>	<b>Uncomfortable (%)</b>
Providing patient education	50%	42.9%	7.1%
Suggesting use of nonprescription medications, eg, paracetamol	21.3%	35.7%	42.9%
Monitoring outcomes of pharmacotherapeutic regimens	64.3%	21.4%	14.3%
Designing and monitoring pharmacotherapeutic Regimes	64.3%	21.4%	14.3%
Detecting and preventing prescription errors	57.1%	28.6%	14.3%
Treating minor illnesses, eg, headaches	21.4%	28.6%	50.0%
Suggesting use of prescription medications to physicians	28.6%	42.9%	28.6%
Suggesting use of prescription medications to patients, eg, antibiotics	21.4%	28.6%	50%



In assessing physician expectations of pharmacist responsibilities, (Table 4) Patient medication education and drug knowledge were unanimously agreed and recognized by physicians to be expected abilities from pharmacists (100% and 93%, respectively) consultative roles, of importance of being knowledgeable to specific drug indications prescribed by the physicians (57.1% agree 21.4% neutral) and being present in rounds for therapy consultations (50% agree, 42.9% neutral) and being involved in resolving any drug-related problems (57.1% agree 35.7% neutral) were also welcomed and expected from clinical pharmacists by majority of physicians surveyed.

While physicians disagreed in views between them toward pharmacists assisting in designing drug-therapy treatment plans for patients (35.7% agree 21.4 neutral 42.9% disagree) and assisting patients in selecting appropriate nonprescription medications (42.9% agree, 21.4% neutral, 35.7% disagree).

**Table 4. Physicians' expectation of pharmacists' professional role n= 14**

<b><u>Physician Expectation</u></b>	<b><u>Agree (%)</u></b>	<b><u>Neutral (%)</u></b>	<b><u>Disagree (%)</u></b>
I expect pharmacists to educate my patients about the safe and appropriate use of their medication.	100%	0	0
I expect pharmacists to be knowledgeable drug-therapy experts.	92.9%	7.1%	0
I expect pharmacists to know the specific indication of each drug I prescribe, even when drugs have more than 1 approved or recognized indication	57.1%	21.4%	21.4%
I expect pharmacists to be involved in resolving any drug-related problems they discover involving patients	57.1%	35.7%	7.1%
I expect pharmacists to assist my patients in selecting appropriate nonprescription medications	42.9%	21.4%	35.7%
I expect pharmacists to assist me in designing drug-therapy treatment plans for my patients	35.7%	21.4%	42.9%
I expect pharmacists to be available to me for consultation when I see patients (eg, during rounds)	50%	42.9%	7.1%

After this assessment, clinical pharmacy services were introduced to the respiratory and allergic diseases clinic, 39 inpatients were covered during the study which was conducted over 60 days, 118 interventions and services were done by the clinical pharmacist mean average interventions per patient was around 2.85. a hundred and two 102 interventions and services (86.4%) were accepted by the physicians , 16 interventions (13.6%) were rejected , and 16 of the accepted were services not directly related to specific patient like drug information DI queries, printed counseling material and in-service education for healthcare team members.

The patients average age was 65.3yrs drugs used in all by them were about (439) from more than 30 different therapeutic categories, mean drugs used by each patient was 11, about half of the patients (51%) were males and (49%) were female patients, as shown in **Table 5**.

**Table 5. Patient's general information**

<b>Patient information</b>	
<b>Age</b>	
Mean	65.3 yrs
Median	69 yrs
Range	20 – 90 yrs
<b>Gender</b>	
Male	20 (51.2%)
Female	19 (48.8%)
<b>Drugs used during hospital stay</b>	
Total # of drugs	439
Range	3 – 20
Median	11
Mean number of drugs used for each patient	11
<b>Interventions</b>	
Number of total interventions	118
Range	0-14
Median	2
Mean interventions per patient	2.85%
Accepted	85%
Rejected	16%

Needed additional drug therapy or stopping unnecessary drugs was the most relevant intervention (21%), followed by dose adjustments(13.5%)and drug treatment recommendations (10.2%), discharge patient education (9.3%), providing drug information (11.9%), initiating lab-works (7.6%), reporting drug-drug interactions (6.8%), and verifying drug orders/doses(5.9%). Less recommendations were related to dose calculation (2.5%),

checking incomplete drug orders (2.5%) drug interval change (1.7%) automatic drug stop orders (1.7%), requesting drug serum levels (1.7%), in-service education for healthcare providers and nurses (1.7%), recommending alternative therapy (0.8%), pharmacokinetics related recommendations (0.8%) (See **Table 6**).

**Table 6.Types of interventions and services done**

Recommendation Code	n (%)
Dosing Regimen Interventions	
Dose Change	16 (13.5%)
Interval Change	2 (1.7%)
D/C Drug (Automatic Stop Order)	2 (1.7)
Drug Change/Add/Delete	25 (21.1%)
Alternate Therapy	1 (0.8%)
Drug Treatment Recommendations	12 (10.2%)
Monitoring Related Interventions	
Pharmacokinetics	1 (0.8%)
Drug Level	2 (1.7%)
Initiated Lab-Work	9 (7.6%)
Adverse Drug Reactions Related Interventions	
Drug Interaction	8 (6.8%)
Check Incomplete Orders	3 (2.5%)
Services & Education	
Discharge Patient Education	11 (9.3%)
In-Service Education	2 (1.7%)
Dose Calculation	3 (2.5%)
Provide Drug Information	14 (11.9%)
Verify Order/Dose	7 (5.9%)

Highest number of recommendations was related to drugs categorized therapeutically as cardiovascular agents 28(23.7%) antimicrobial agents were the second 23 (19.5%) while interventions and services related to bronchodilators and inhalers were the third 22(18.6%) (due counseling services mainly 18(88.8%)) followed by anticoagulation anti-thrombotic agents 12 (10.2%) respectively (**Table 7**).

**Table 7.therapeutic classification of drugs related to interventions**

<u>Therapeutic class</u>	<u>n (%)</u>
Drugs commonly used in RD	
Bronchodilators and inhalers	22 (18.6%)
Antibiotics	23 (19.5%)
Drugs used commonly for non-respiratory diseases	
Anticoagulants /antithrombotic	12(10.2%)
Cardiovascular agents	28 (23.7%)
Anti-inflammatory drugs	1 (0.85%)
Diuretics	4 (3.4%)
Electrolyte replacement drugs	4 (3.4%)
Essential minerals	1 (0.85%)
Drugs for hyperlipidemia	2 (1.7%)
Thyroid replacement	1 (0.85%)
BPH treatment agents	2 (1.7%)
Cough suppressants	1 (0.85%)
Analgesics	2 (1.7%)
Vitamins	2 (1.7%)
Gastro-intestinal medications	1 (0.85%)
Dietary supplements	1 (0.85%)
Psycho-therapeutic agents	2 (1.7%)
Sedative hypnotic agents	4 (3.4%)
Others	5 (4.2%)

An independent clinical committee assessed the clinical significance (**Table 8**) and effect of interventions made by clinical pharmacists on outcomes. Outcomes of the interventions were categorized as those to avoid adverse effects or toxicity 37(31.4%), improve therapeutic effects 29 (24.6%) Increased quality of care 23 (19.5%) provided information 22 (18.6%), were less of interventions led to decrease cost 3 (2.5%) or were prevented medication errors 2 (1.7%) and provided services 2(1.7%) while none of the interventions were avoided allergic reactions.

**Table 8. Proposed effects of interventions on outcomes**

<b>Outcome</b>	<b>(%)</b>
Decrease Cost	3 (2.5%)
Increase Quality	23 (19.5%)
Avoided ADR/Toxicity	37 (31.4%)
Prevented Med Error	2 (1.7%)
Improved Effect	29 (24.6%)
Provided Service	2 (1.7%)
Provided Information	22 (18.6%)

Table 9 lists physicians' actual experience with the clinical pharmacists surveyed after the end of the study. The physicians agreed that pharmacist being a reliable and confident source of drugs general information 5(100%) and also reliable source of clinical drug information 4(80%). They also agreed with pharmacists frequently asking them to clarify drug therapy objectives and indications for the patients 5(100%) and informing them when their patients have clinical problems with their medication 5 (100%) while they mostly agreed with pharmacists taking personal responsibility for resolving any drug related problems they discover (3 agree 60% 2 neutral 40%) also three physicians agreed with that pharmacist provided them with more cost-effective alternatives to the drugs they prescribed (60%) , while one physicians disagreed with that (20%) and one was neutral (20%).

Also physicians reported that the pharmacist counseled their patients but not usually (60% agreed 40% neutral) and all (100%) were neutral about that the pharmacist frequently noticed them that their patients have some problems with their medications.

**Table 9. Physicians' actual experience with a clinical pharmacist (n=5)**

<b><u>Physicians' experiences</u></b>	<b>Agree (%)</b>	<b>Neutral (%)</b>	<b>Disagree(%)</b>
In my experience, pharmacists are a reliable source of general drug information.(ie, specific facts about drugs, which can be found in standard references)	100%	0	0
Pharmacists routinely counsel my patients regarding the safe and appropriate use of their medications	60%	40%	0
In my experience, pharmacists are a reliable source of clinical drug information.(ie, information regarding the clinical use of drugs in specific situations)	80%	20%	0
Pharmacists routinely inform me about more cost-effective alternatives to the drugs I prescribe	60%	20%	20%
In my experience, pharmacists appear willing to take personal responsibility for resolving any drug-related problems they discover	60%	40%	35.7%
Pharmacists routinely inform me if they discover clinical problems with my prescriptions	100%	0	0
Pharmacists frequently ask me to clarify for them the drug-therapy objectives I have in mind for my patients	100%	0	0
Pharmacists frequently let me know that my patients have experienced some problem with their medication	100%	0	0

Comparing physicians who had experience with clinical pharmacist to those who rarely or never had so , in terms of comfort with pharmaceutical care duties and their expectations of clinical pharmacists , physicians of interventional group reported that they are comfortable of pharmacist educating their patients (100%),and detecting and preventing prescription errors (100%), they were mostly comfortable with monitoring outcomes of pharmacotherapeutic regimen by clinical pharmacists (80%) and pharmacists suggesting use of prescription medications to doctors (80%), they were moderately comfortable with involving in designing therapeutic regimens duties of pharmacists (80%) and them suggesting nonprescription medications to patients (60% comfortable, 40% moderately comfortable) while they still resist and feel uncomfortable with any prescribing duties of

either treating minor illnesses (100%) or suggesting prescription medications to patients (80%).

They all agreed with pharmacists role in educating their patients (100%), being available for consultations in healthcare provider teams medical rounds (100%), they recognize them to be knowledgeable drug therapy experts (100%) and that they should know each drugs indication in each patient (100%) , majority agreed with roles of resolving drug related problems they discover (60% agree 40% neutral ) and assisting in designing drug-therapy treatment plans for physicians patients (60% agree, 40% neutral ) while they felt neutral toward pharmacists suggesting nonprescription medications for patients (80%) (**Table 9**).

## 7. Discussion

Clinical pharmacy services and practice are obviously not common in Turkey and northern Cyprus. Very few number of physicians (3), had previous contact with a clinical pharmacist, of these, two physicians reported that their contact with a clinical pharmacist was rare, while one physician obtained his qualifications and practice from countries other than Turkey and Cyprus, which clears out that the practice of clinical pharmacy, is rare in Cyprus. This may justify why 40-50 % did not recognize or feel comfortable with pharmacist roles of monitoring therapy plans, preventing errors and solving them when occur, and assisting in rounds and designing treatment plans.

Studies done for decades in developed countries, showed that lack of exposure to pharmacists activities is the main reason attributed to lead to discomfort making physicians reluctant to approve and accept more clinical duties for pharmacists.[139,140]

For example in china, where many pharmacists practice clinical pharmacy in clinics and hospitals, a recent study done to evaluate attitudes toward clinical pharmacy services in urban general hospitals in China(china,2014) reported that more than 83.3% of physicians surveyed (n=646) have frequent interactions with clinical pharmacists, and had more than 80% comfort with pharmacists involving in, rounds ,designing therapeutic plans, assisting in treatment of complex cases , and in prescribing generally. While around 84% comfort was reported to activities of monitoring therapeutic plans and preventing prescription errors and scanning and preventing adverse drug reactions.[141] In the Netherlands a study investigating physicians and pharmacists opinions toward pharmacists' professional duties, researchers found that over 80% of the sampled healthcare professionals agreed that pharmacists should have an input in the patient's pharmacotherapeutic plan and also should participate in the pharmacotherapy audit meetings.[142]



However of this, it's positive that many had high expectations, were almost all physicians (92%) recognize pharmacist to be knowledgeable drug-therapy experts. And (100%) accept the role and importance of clinical pharmacists in patient education, while near to 60% accepted roles of resolving drug-related problems and monitoring pharmaco-therapeutic plans, and around 43% recognize the importance of involving clinical pharmacists in rounds and in designing patients care plans, compared to studies carried elsewhere on physicians perceptions, expectations and experience where researched found only 35.7% comfort and 45.8% moderate comfort to monitoring activities and preventing errors, while 24.9% and 45% comfort and moderate comfort respectively was reported to consultation services , presence in medical rounds and assisting in therapeutic plans. Only 33% recognized such services as pharmacist expected roles and 62% supported pharmacist's patient education duties.[143]

Similar numbers were observed in studies done in Qatar and Kuwait regarding physicians view and expectations of pharmacist role,[143-145] though in Qatar physicians widely supported patient education activities (96.6%) while (77%) acceptance was observed in Kuwait.[144,145]

Regarding prescribing activities, though much less resistance is observed in developed countries (only 45.9% uncomfortable to clinical pharmacists having some prescribing authority for treating minor diseases. And 40% feeling comfortable to pharmacist managing outpatient clinic for anticoagulant therapy, treating chronic diseases, and having the right to continue or revise the prescription under authorization from physicians [141] but though it's universally well-known and common that it's unlikely that physicians agree with prescribing authorities given to pharmacists [140, 146], as it also seen in this study to (47% uncomfortable, 31% moderately comfortable) and other studies Kuwait, Jordan and Qatar.[143-145]

Up to here we can conclude though many physicians have minimum interaction and experience with clinical pharmacist, and thus some misperceptions towards some core clinical pharmacists duties, but still high expectations were obvious and physicians appeared to have highly regard pharmacists as knowledgeable drug therapy experts (92%) and many expect them to part of administering care to patients while majority agree with the need to educate patients about the safe and appropriate use of medications. This is a good sign comparing to other countries and to the novelty of this practice in Cyprus.

Though the sample was very low compared to other studies done on perception and thus we cannot generalize these observations or significantly compare them to other done studies indicating to the necessity to carry well designed studies with a representative sample size. Such studies are ultimately important to clinical pharmacist and pharmacy faculties and pharmacy organizational bodies in Cyprus, so to guide them to opportunities and threads in attaining collaborative work relationship with physicians while developing pharmacy practice in Cyprus.

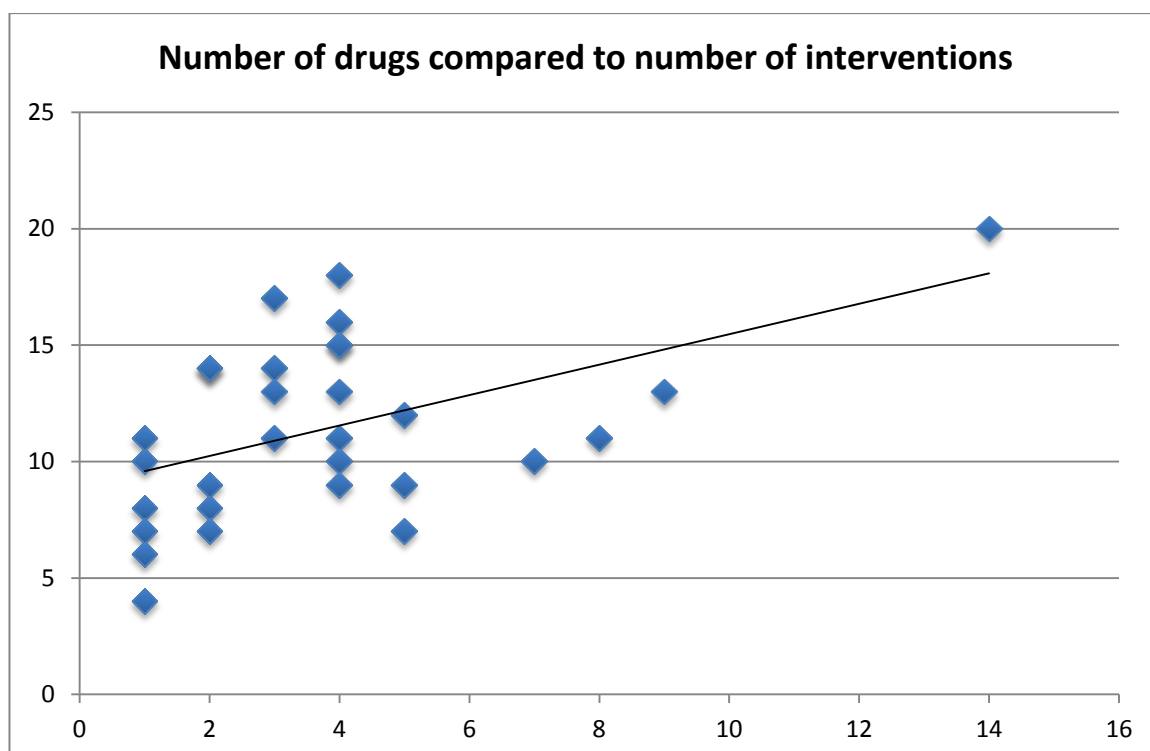
In the interventional part of this study, clinical pharmacy services were introduced to the respiratory and allergic diseases clinic in NEU hospital, clinical pharmacy services promote rational use of medications and has positive well documented effects on most pathologies, (A-Z) an intervention by a pharmacist which is regarded as a near-miss incident, can be defined as any action done by the pharmacist that directly result in a change in a patients management or therapy [147]. Implementing CPS's resulted in 118 different interventions were done on average of 2.85% per patient. Number of the clinical pharmacist's interventions accepted by the physicians and types of drug related problems that requires clinical pharmacist's interventions were the main outcomes.

A relatively high degree of acceptance of the interventions as reported 86% which is comparable to studies done on implementing clinical pharmacy services in different wards and clinics in the united states 95%( obtained from a review summarizing the available evidence regarding the role and impact of clinical pharmacy services in the care of solid organ transplant ) [148] where studies conducted in Europe reporting acceptance rates of clinical pharmacy services revealed rates between 69 and 89 % , which is considered high [149-152] while studies also reported 88% in Turkey [153], 87% [154] 69.4 % [155] elsewhere.

Such a high rate indicates that the interventions have been timely and relevant for the physicians, it also supports that a trust relationship existed and a CWR between the physicians and the pharmacist what lead to this rate. [156]

Mean average age of the patients was 65. yrs , indicating that elders were vast majority of the patients , also polypharmacy was obvious where drugs used for the patients during their stay ranged between 4-20 and mean drugs used by patient was 11, this is comparable to a

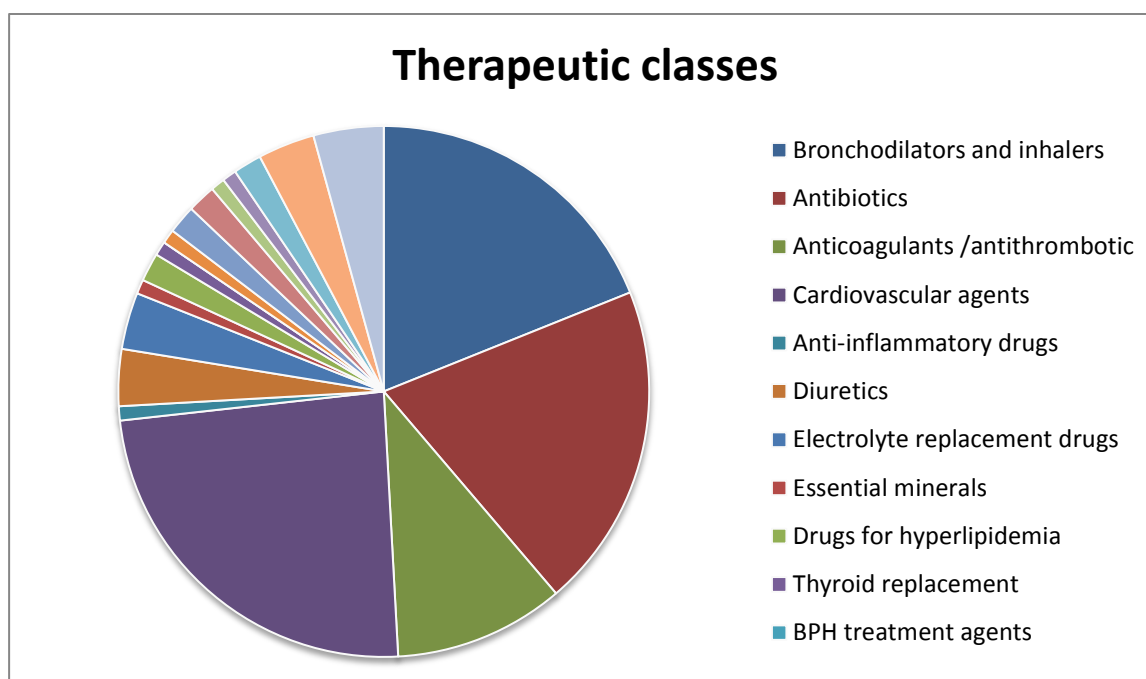
study held in Denmark where patients age ranged between 26–97 years old and drugs used ranged between 4–22 drugs per day [150], previous studies report 85% of those 65 years old and over to have at least one chronic disease, while 30% of them have 3 or more chronic diseases [156], interventions generally was noted to increase significantly with increasing number of medications per patient, while clinical pharmacists are regarded as a key approach for optimization of prescribing in this age group (fig 1) [157].



**Fig 1:** correlation between number of drugs and number of recommendations in individual patients.

The most frequent types of interventions were "drug started/stopped/changed" 21.1% what reflect the common typical focus areas of rational drug therapy in the elderly and in polypharmacy patients [158,159]. Following in frequency was "dose adjustment" 13.5% which also goes with people when getting older start to loose hepatic and renal function what always necessities dose adjustment.

Of interest, cardiovascular agents were the most reported therapeutic category which interventions were mostly related to (around quarter of all interventions), a finding also obtained from a Danish study (also nearly a quarter) though they sampled from all ICU patients, put the real interesting is a recent (feb,2014) printed study conducted by Swedish researchers where they studied MI Mortality in COPD Patients, and found One-year mortality in MI patients which is significantly higher in those with underlying chronic obstructive pulmonary disease (COPD) than in patients with no underlying lung disease,. Strikingly however, this increased risk falls substantially in analyses that controlled for both comorbidities and treatment patterns, pointing to a significant under-treatment of cardiovascular disease in this group. [160]



**Figure 2:** a pie chart showing therapeutic classifications of drugs related to each interventions showing cardiovascular agents to be must related agents to interventions followed by Antibiotics and bronchodilators respectively.

It's reasonable to think that this is related, in term that we found in this study that there is in general many interventions done in a respiratory diseases clinic these diseases include reactive airway diseases of asthma and COPD and others and we found that majority of interventions of optimizing drug use were related cardiovascular agents which is found that specific disease group inside this sample are likely under treated for MI the major cardiovascular event , but such a generalization could be done and is not feasible in the case

of this study because of the presence of many confounding variables, need for specifically targeting related group and more specifications and more characterization of each intervention done is needed so to draw such a correlation with that study held in Sweden .

Second class of medications which interventions were mostly related to was antibiotics (19.5%) and inhaled bronchodilators (18.6%), this are drugs most commonly used in such a clinic (asthma, COPD, and pneumonia) and justifies the great number of interventions related to them, added to that counseling activities were attributed to 88% of recommendations concerning inhalers while recommendation of dose changes was the second most leading type of total recommendations done in heart of that is those related to antibiotics mainly due to renal or hepatic impairment which is common for the sample age group, showing that regardless of the predicted heavy use of antibiotics in a respiratory clinic, majority of interventions were related to drug doses not to drug regimen used which may indicate physicians restriction to national and international guidelines for antibiotics use for different cases which were revised by the clinical pharmacist for every and each case encountered during the study period, and thus indicates rational drug use concerning antibiotics which is critical and important in terms of attenuating emergence of resistance to antibiotics and also in terms of cost-effectiveness were I.V antibiotics are costly and thus require rational use restricted to need.

Anti-coagulant and antiplatelet were the fourth leading class of medications interventions were related to which was composed mainly of initiating and proper dosing DVT prophylaxis agents, and was mostly accepted.

Comparing acceptance rate of drugs commonly used in respiratory clinics i.e. antibiotics, and bronchodilators to others e.g. cardiovascular agent, anticoagulation therapy, etc. showed significant difference in the way they were accepted, 66.7% of accepted interventions were related to drugs not commonly used or initiated by respiratory diseases clinics, which suggest that the efficacy of clinical pharmacists maybe due to being drug experts in many classes of medications, and thus may reduce incidence of DTP related to comorbidities other than the acute complains which are constantly under the focus of the healthcare providers .

Also comparing acceptance rates to types of recommendations, significant difference in the way interventional recommendations were accepted was noticed compared to services provided by the pharmacist ( $p= 0.004$ ). All suggested services were accepted indicating to the importance of pharmacists being initiative and the appreciation of physicians to such collaborative relationship, pharmacists actually shouldn't wait others to seek their services but rather should act as leaders and offer their services to others who will appreciate and respect it. Services included DI queries, printed patient education material, and CME's activities on inhalation techniques and advances in hypertension treatment guidelines for nurses and healthcare providers.

According to similar studies done to evaluate clinical pharmacist interventions, outcomes and impact of the study were demonstrated by the number of interventions, their acceptance rate, and clinical importance. In assessing such outcomes many ways are used in different studies categorized generally into outcome measures that are explicit (criterion-based) or implicit (judgment-based). [150]

In this study we used implicit approaches, where a clinician uses information from the patient and published work to make judgments about outcomes, though sensitive, and preferred mostly, but also they are time-consuming, depends on the user's background knowledge and attitudes, and can also have low reliability, while other methods are costly require follow up at different centers and need much cooperation and support, thus There is no ideal measure, but the strengths and weaknesses of both approaches should be considered.[157]

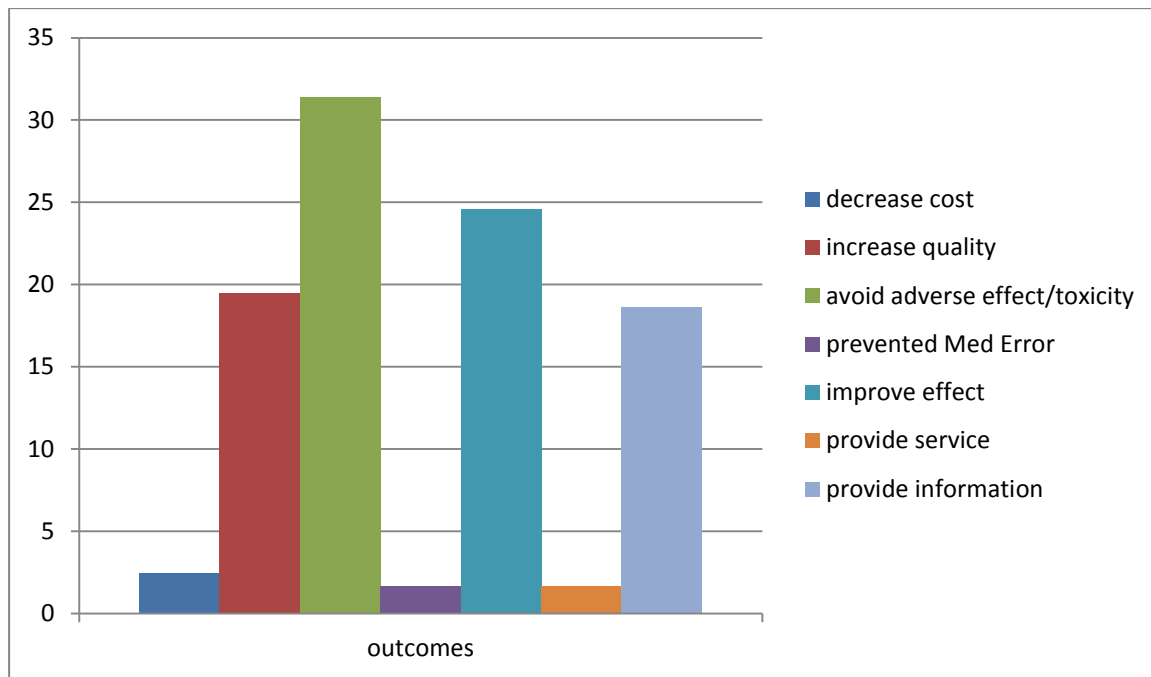


Figure 3. Outcomes of carried interventions on patients

Thus for the assessment of the interventions, a multidisciplinary independent clinical committee (two physicians & one clinical pharmacist), was responsible to review and assess the significance of interventions, a method or an approach utilized by other investigators evaluating clinical pharmacists' interventions.[160-162]

A detailed interventions outcomes criteria was obtained from literature review and adopted for this purpose,[155] six main outcomes were assigned, either to increase cost , decrease cost, increase quality of care prevent adverse effect or toxicity improve therapeutic effect, avoid allergic reaction , provide information, or provide a service.

Interventions done by the pharmacist were assigned mainly (31%) to prevent adverse events or drug toxicity, secondly were interventions that improve therapeutic effects (24.6%) followed by those that increase quality of care(19.5), and provided information (18.4).

The committee had assigned outcomes and validated all interventions, though reported some defects regarding the need to use of scientific named of drugs in documentation and individual cases need for further information, some missing daily blood pressures and diagnostic information of some cases e.g. chest X ray for a patient diagnosed with pneumonia, but defects were regarded minor errors and did not affect results.

On the end of the study a survey of eight items was carried to evaluate physician's experience, also they were required to fill the same tool used at the start of the study to evaluate comfort and expectations for pharmacist roles pharmaceutical care activities, due to low number of physicians in investigational group (3 physicians), two physicians from the pediatric clinic of the same hospital who had experience with the clinical pharmacist beyond the start of this study were also surveyed for their experience with the clinical pharmacist who stayed a comparable short period (45 days) in their clinic.

Physicians showed high degree of comfort towards pharmaceutical care activities in general, they seemed much more understandable to different pharmaceutical care aspects of monitoring and preventing errors, consultation services and presence in medical rounds and assisting in therapeutic plans and highly perceived such activities.

To their experience, pharmacist routinely counseled their patients regarding the safe and appropriate use of their medications (60%), routinely informed them if more cost-effective alternatives existed (60%), pharmacists appear willing to take personal responsibility for resolving any drug-related problems they discover (60%).

Also they reported that Pharmacists routinely inform them if they discovered clinical problems with prescriptions (100%), frequently asked physicians to clarify for them the drug-therapy objectives they have in mind for their patients (100%) and frequently let them know if patients have experienced some problem with their medication.

To their experience, all physicians regarded pharmacists are a reliable source of general drug information and 80% regard them as also a reliable source of clinical drug information.



**Table 10 &11** compare responses of physicians regarding degree of comfort and expectations to their specific responses on baseline, though we cannot draw generalizations of this due to low sample size, what necessities further studies.

**Table 10.** Degree of comfort before and after the introduction of CPS.(n=3).

Pharmacists' duty	CA		Mod.CA		Un.CA	
	Baseline	End	Baseline	End	Baseline	End
Providing patient education	66%	100%	34%	0	0	0
Suggesting use of nonprescription medications, eg, paracetamol	33%	66%	34%	34%	33%	0
Monitoring outcomes of pharmacotherapeutic regimens	66%	100%	34%	0	0	0
Designing and monitoring pharmacotherapeutic Regimes	34%	0	0	100%	66%	0
Detecting and preventing prescription errors	66%	100%	34%	0	0	0
Treating minor illnesses, eg, headaches	0	0	0	0	100%	100%
Suggesting use of prescription medications to physicians	33%	100%	34%	0	33%	0
Suggesting use of prescription medications to patients, eg, antibiotics	0	0	0	0	100%	100%

**Table 11.** RD clinic physician's expectations before and after study. (n=3)

<u>Physician Expectation</u>	Agree (%)		Neutral (%)		Dis-agree (%)	
	Baseline	End	Baseline	End	Baseline	End
I expect pharmacists to educate my patients about the safe and appropriate use of their medication.	100%	100%	0	0	0	0
I expect pharmacists to be knowledgeable drug-therapy experts.	100%	100%	0	0	0	0
I expect pharmacists to know the specific indication of each drug I prescribe, even when drugs have more than 1 approved or recognized indication	66%	100%	34%	0	0	0
I expect pharmacists to be involved in resolving any drug-related problems they discover involving patients	34%	100%	66%	0	0	0
I expect pharmacists to assist my patients in selecting appropriate nonprescription medications	33%	0	34%	100%	33%	0
I expect pharmacists to assist me in designing drug-therapy treatment plans for my patients	33%	66%	34%	34%	33%	0
I expect pharmacists to be available to me for consultation when I see patients (eg, during rounds)	100%	0	100%	0	0	0

**Strengths and limitations:**

To our knowledge, this is the first study to evaluate physicians perception and expectations in TRNC and Turkey, also it is the first study to implement clinical pharmacy services in Cyprus, of interest was also that this study reported not only the perceptions or effect on patients but showed practical impact of clinical pharmacy on perceptions and patients and evaluate after experience of physicians.

Also many positive interventions were done for patients during the study resolving DTP and providing direct services and care to patients, CME's and diverse drug information was provided, high degree of acceptance of interventions was achieved and positive perceptions and increased awareness of pharmacist roles and responsibilities was done during the study.

But though, many limitations had lead less beneficial outcomes for this study, of this, low sample size was of great negative effect on the study and resulted in many interesting but un-generalizable idea's regarding perceptions expectations and of course experience of physicians with pharmacist, while also the short length of the interventional study lead to less than the expected outcomes .

Also regarding the interventional part of the study, limited number of pharmacist introducing the CPS's (only one) and linguistic barriers resulted in less maximization of interventions as patient education and medication history review, while (3) physicians could not response to the questionnaire due to language difficulties.

Also the design of the study, tools adapted from other studies were not much descriptive and suitable for this sample size, for example for outcomes; better tools could be used in future studies to evaluate interventions and DTP's (e.g. The PCNE)

It is also of mention that NEU hospital is regarded the leading hospital in Cyprus and its healthcare providers are regarded much talented and competent, this can lead to bias if results are generalized for all hospitals in Cyprus, and better picture could be drawn if the study was multicenter study with representative sample size and also control group.

## 8. Conclusion.

Clinical pharmacy is of much proved benefit in many different setting leading to optimization of drug therapies ,reducing and solved drug related problems ( DRP's) and preventing potential side effects of drugs , physicians response and collaboration is much crucial in achieving this rationalization of drug use duty done by the clinical pharmacists . such a successful collaborative work relationship could be emerged first by well studying the current perceptions of healthcare providers and resolving miss perceptions collaboratively by introducing a good practical model of practice and demonstrating benefits of such a practice professionally by well documentation and record, ease of frequent contact between physicians and pharmacist is one of leading causes of misperception as reported in many studies.

In this study, relatively high expectations and encouraging perception were reported from physicians towards clinical pharmacy and pharmaceutical care duties, though most physicians never experienced such activities in their settings , these perceptions were even more improved after piloting a study were clinical pharmacy services where introduced into a respiratory clinic for a short period , and experience was evaluated then after , yet physicians were less likely to accept any prescribing activity from the pharmacist ,and also still these positive results cannot be generalized due to small sample size.

High rate of acceptance was also reported to 118 interventions introduced by the clinical pharmacist which may reflect the positive results obtained from the small sized sample surveyed, interventions were mainly related to drugs not commonly prescribed by the clinic, cardiovascular agents being leading therapeutic class related to interventions while adding and stopping or changing medications plus dose adjustments were the main types of interventions encountered. This may require further studies to evaluate degree of irrationality regarding cardiovascular agents in COPD patients to investigate if this finding is related to recent studies reporting one year higher risk of MI in this group due under-treatment.

Significance differences were noted between acceptance of services and interventions while significant correlation also exists between number of interventions and drugs used for each patient.

Majority of the covered patients had polypharmacy while clinical pharmacist resulted in 2.9 mean amounts of interventions per patient, and majority were elders (mean = 65 yrs.) with mean number of medications for each person to be 11.

Physicians perceptions after the study shows that it was positively affected by the experience of clinical pharmacy services , though also baseline survey also showed good perceptions and general welcoming , what mops the way and gives a good opportunity for pharmacy bodies and pharmacy faculties in Cyprus for implementing advanced pharmacy practices and pharmaceutical care in Cyprus.

Further better designed studies in terms of control group and sample size should be carried to more sharply investigate physicians perceptions before and after introducing pharmaceutical care while more implementation of pharmaceutical care and clinical pharmacy practice is important in other wards for longer periods so to compare such results to this study findings and more even provide and proof clinical pharmacy efficiency and advantages, future studies may also cover the impact on cost and degree of cost-effectiveness of introducing clinical pharmacy services .

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**Appendix I: Questionnaire for Evaluating Physician's Perceptions, Expectations & Experience.**

**Section I: Personal Information**

1. In which age group are you?
- ☐ Less than 35 yr
  - ☐ 36-46 yr
  - ☐ More than 47 yr
2. Gender:
- ☐ Male
  - ☐ Female
3. Nationality:
- ☐ Cypriot
  - ☐ Turkish mainlander
  - ☐ Other
4. Country where medical qualification was obtained?
- ☐ Turkey
  - ☐ Cyprus
  - ☐ US
  - ☐ Eastern Asia
  - ☐ Western Europe
  - ☐ Eastern Europe "including Russia"
  - ☐ Other, please specify: .....
5. Place of work : ☐ Near East Hospital  
☐ Others .....
6. Current position:
- ☐ Trainee (the first year of training after graduation)
  - ☐ Junior (first and second year resident)
  - ☐ Senior (third and fourth year resident)
  - ☐ Fellows
  - ☐ Consultant
7. Current area of practice:
- ☐ Internal Medicine
  - ☐ Pediatrics
  - ☐ Surgery
  - ☐ Obstetrics & Gynecology
  - ☐ Ear, nose, throat
  - ☐ Dermatology
  - ☐ Others

## Section II: Frequency and reasons of interactions between physicians and pharmacists:

7. Frequency of interactions with pharmacists generally:
- ☐ Never/rarely
  - ☐ Once a week
  - ☐ Once a day/more
8. Ever worked with a clinical pharmacist before?
- ☐ Never
  - ☐ Yes, I did work with a clinical pharmacist before
9. Reasons for interactions (more than 1 choice can be checked)
- ☐ Drug-availability queries
  - ☐ Side-effects queries
  - ☐ Drug-alternative queries
  - ☐ Drug- interaction queries
  - ☐ Others.

## Section III: Physicians' degree of comfort with pharmacists providing different pharmaceutical care services.

Pharmacists' duty	Comfortable	Moderately comfortable	uncomfortable
Providing patient education	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Suggesting use of nonprescription medications, eg, paracetamol	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Monitoring outcomes of pharmacotherapeutic regimens	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Designing and monitoring pharmacotherapeutic Regimes	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Detecting and preventing prescription errors	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Treating minor illnesses, eg, headaches	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Suggesting use of prescription medications to physicians	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Suggesting use of prescription medications to patients, eg, antibiotics	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

## Section IV: Physicians' expectation of pharmacists' professional role

<b>Physician Expectation</b>	
I expect pharmacists to educate my patients about the safe and appropriate use of their medication.	<input type="radio"/> Agree <input type="radio"/> Neutral <input type="radio"/> Disagree
I expect pharmacists to be knowledgeable drug-therapy experts.	<input type="radio"/> Agree <input type="radio"/> Neutral <input type="radio"/> Disagree
I expect pharmacists to know the specific indication of each drug I prescribe, even when drugs have more than 1 approved or recognized indication	<input type="radio"/> Agree <input type="radio"/> Neutral <input type="radio"/> Disagree
I expect pharmacists to be involved in resolving any drug-related problems they discover involving patients	<input type="radio"/> Agree <input type="radio"/> Neutral <input type="radio"/> Disagree
I expect pharmacists to assist my patients in selecting appropriate nonprescription medications	<input type="radio"/> Agree <input type="radio"/> Neutral <input type="radio"/> Disagree
I expect pharmacists to assist me in designing drug-therapy treatment plans for my patients	<input type="radio"/> Agree <input type="radio"/> Neutral <input type="radio"/> Disagree
I expect pharmacists to be available to me for consultation when I see patients (eg, during rounds)	<input type="radio"/> Agree <input type="radio"/> Neutral <input type="radio"/> Disagree

## Section IV: Physicians' experience with pharmacists providing different pharmaceutical care services.

<b>Physicians' experiences</b>	
In my experience, pharmacists are a reliable source of general drug information.(ie, specific facts about drugs, which can be found in standard references)	<input type="radio"/> Agree <input type="radio"/> Neutral <input type="radio"/> Disagree
Pharmacists routinely counsel my patients regarding the safe and appropriate use of their medications	<input type="radio"/> Agree <input type="radio"/> Neutral <input type="radio"/> Disagree
In my experience, pharmacists are a reliable source of clinical drug information.(ie, information regarding the clinical use of drugs in specific situations)	<input type="radio"/> Agree <input type="radio"/> Neutral <input type="radio"/> Disagree
Pharmacists routinely inform me about more cost-effective alternatives to the drugs I prescribe	<input type="radio"/> Agree <input type="radio"/> Neutral <input type="radio"/> Disagree
In my experience, pharmacists appear willing to take personal responsibility for resolving any drug-related problems they discover	<input type="radio"/> Agree <input type="radio"/> Neutral <input type="radio"/> Disagree
Pharmacists routinely inform me if they discover clinical problems with my prescriptions	<input type="radio"/> Agree <input type="radio"/> Neutral <input type="radio"/> Disagree
Pharmacists frequently ask me to clarify for them the drug-therapy objectives I have in mind for my patients	<input type="radio"/> Agree <input type="radio"/> Neutral <input type="radio"/> Disagree
Pharmacists frequently let me know that my patients have experienced some problem with their medication	<input type="radio"/> Agree <input type="radio"/> Neutral <input type="radio"/> Disagree

**Appendix II: Independent Multi-Disciplinary Committee Declaration Letter**

**Appendix III: Institutional Review Board (IRB) Ethical Approval Letter.**