NARRATIVE REVIEW

A snapshot of the global policies and practices of medicine use reviews by community pharmacist in chronic diseases: A narrative review

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Abstract

Medicine use review is a tool to improve medication adherence and safety. Current narrative review was planned to explore global policies and practices of medicine use review by community pharmacists in chronic diseases and its impact and way forward for low- and middle-income countries. Key words, such as ″medicine use review″, ″medication therapy management″ and ″community pharmacy″ were used for search on PubMed and CINAHL databases for articles published from 2004 to 2019. Medicine use review has opened an avenue of ongoing collaboration between community pharmacists and general practitioners. High-income countries have witnessed a gradual yet cautious adoption of these services through effective policy shift. In terms of practices and impact, the situation in high-income countries was promising where on an average ″type-II″ medicine use review was widely in practice and had improved clinical, humanistic and economic outcomes in chronic disease. However, in low- and middle-income countries, a paucity of effective policies was noted. Nevertheless, an emergent recognition of the potential of community pharmacists to contribute to the management of chronic diseases was evident.

Keywords: Community pharmacist, Medicine use review, Pharmacy practice and policy, Collaboration, Low- and middle-income countries, Chronic diseases.

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Introduction

Global Burden of Chronic Diseases

In the 21st century, chronic diseases are considered a grave threat to healthcare systems because of human miseries, hardships and damage they levy on the economic fabric of the countries. This is of more relevance for low- and middle-income countries (LMICs) which share 85% burden of chronic diseases of the globe. In context of this review, chronic diseases include, cardiovascular diseases, like hypertension (HTN) and stroke, chronic respiratory diseases, like asthma and chronic obstructive pulmonary disease (COPD), cancer and diabetes.[1] Medicines are the most common, repeated and continual interventions in chronic diseases throughout life and hence receive vital importance. Spending too much on medicines indicates healthcare system's inefficiency.[2] Zermansky was the first to emphasize on the need of regular checks on medicine use in chronic diseases.[3] He pointed out the lack of peer review of medicine use as the core reason of therapy failures in chronic patients whose prescriptions have not been reviewed year after year. Pharmaceutical Care Network Europe (PCNE) has recently defined "medicine use review" (MUR) as "a structured evaluation of a patient's medicines with the aim of optimising medicines use and improving health outcomes. This entails detecting drug-related problems and recommending interventions".[4] Table-1 enlists various types of MUR and their salient features to identify the level of operations in a community pharmacy. Type-I review is a normal routine practice during dispensing, while type-II involves a much-detailed version of type-I with a major focus on medicine use process to improve adherence. Type-III review is the most advanced level which requires clinical notes and one-to-one patient

Table-1: Characteristics of different types of medication reviews.

MUR	Objective	Focus	Patient Interaction	CP's access to patient information	Level
Type-I	Technical review of the prescription.	Medicine	No	Not necessary	Basic
Type-II	Improvement of patient adherence to drug therapy.	Medicine taking behavior of the patient	Yes	Limited, Occasional	Intermediate
Type-III	Clinical review of the medicines.	Medicine in context of disease	Yes	Extensive, Always	Advance

MUR=Medication Use Review, CP= community pharmacist.

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meeting with focus on medicine as well as diseases or multiple diseases to optimise medication therapy.[5]

Need and significance of MUR in chronic diseases

There are compelling reasons that signify the need of a MUR in chronic diseases:

a) More than 50% of prescription drugs in chronic diseases are not taken as desired which leads to therapy failure.[6]

b) Non-adherence to medications in chronic diseases is a global concern and considered a precipitating factor for poor disease management. It wreaks $100 billion loss to the United States of America (USA) healthcare resources annually.[7]

c) Chronic diseases, especially in older age, have high potential for medication errors due to complexity of medication regimen, patient's functional status, disease's prognosis, severity and co-morbidities.[8] These errors are largely avertable and can be forestalled through MUR and save $4.75 trillion per year globally.[9]

Thus, chronic diseases require MUR which covers essential aspects of medicine use process, such as consistent monitoring, documentation and regular follow-ups across lifetime to improve quality of life.

Community pharmacist and MUR: "a potential resource or a lost opportun ity"?

Pharmacists constitute the third largest healthcare professional body in the world. They acquire professional education and training to provide services to ensure optimal use of medications. In developed countries, since the 1980s, pharmacists in hospitals started taking part in reviewing medications and recommending to general practitioners (GPs) any alteration in medicines, if required.[10] However, until recently, the approach of involving a pharmacist in direct patient care was not translated into practice for community pharmacists (CPs). The ease of access, from a patient perspective, makes community pharmacy a preferred place for activities related to preventive health, health promotion, patient education and self-management in the context of chronic diseases.[11] Furthermore, patients do not have to wait in long queues or need to worry about the short operating hours. Thus, incorporating CPs in the chronic care team would likely to solve many of the -related problems (DRPs) cited earlier.

Pharmaceutical drug care to MUR: from philosophy to practice

The Hepler's classical concept of ″pharmaceutical care″ in the 21st century involves consistent monitoring and MUR of an individual patient to optimise the therapy for the benefit of the patient.[12] In developed countries, the concept of pharmaceutical care has evolved into the MUR which is of high relevance in practice of chronic disease patients. However, the nomenclature for the concept of MUR varies across the globe (Table 2).[13,14] Thus, different terminologies are used to describe MUR services, provided generally by a CP, may have technical differences, but generally have a common objective of optimal management of medicines to maximise the therapeutic effects through continuous surveillance. Nevertheless, whatever the nomenclature in a country, from a technical point of view, some components of MUR remain common, such as prescription review to assess any inappropriate use of medicines, like over, under or misuse, documenting a personalised care plan and written follow-up to provide adherence support based on individual patient's needs. However, it is also true that the scope of practice, in the context of involving CPs in patient care, varies formidably in different parts of the world.[15,16]

Table-2: Different Nomenclature to describe Medicine Use Review/ pharmaceutical care in various countries.

Country	Nomenclature used to describe Medicine Use Review/ Pharmaceutical Care
UK	Medicine use review, New medicine service, Medicine reconciliation, Medicine optimization, Chronic Medication Review
USA	Medication therapy management, Comprehensive medication review, Drug utilization evaluation
Australia	Home medication review, Domiciliary Medication Management Reviews, Residential Medication Management Review, Medscheck
Canada	Medcheck
Switzerland	Poly medication check
Spain	Medication review with follow-up
Netherlands	Medication Monitoring and Optimization
New Zealand	Medicine adherence services, Medicine use review, pharmacy long term conditions services, comprehensive medicine management, medicine therapy assessment, community pharmacy anticoagulation management services
Belgium	New medicine service
Brazil	Pharmacotherapy follow-ups

UK: United Kingdom; USA: United States of America.

Objective

Current narrative was planned to explore global policies and practices review of MUR offered by CPs in chronic diseases to inform relevant stakeholders about the current trends, vision and models of chronic care operating through community pharmacy.

Methods

This narrative review of the literature used a combination of key words and MESH words, such as ″medicine use review″, ″drug use review″, ″medication therapy management″ and ″community pharmacy″ for search on PubMed and CINAHL/EBSCO databases for articles published from 2004 to 2019 (Appendix, Section B). The

search was meant to retrieve studies focussing on the policy, practice and impact of MUR in chronic diseases management published in English language. Studies were excluded if conducted at a setting other than community pharmacy, or merely described students' attitude or perception (Appendix, Section A, Flow chart of the articles retrieval).

Result

There were significant differences in how CP was being utilised in different parts of the world regarding MUR services in chronic diseases. The developed countries have witnessed a gradual yet cautious adoption of MUR through effective policy shift which has positively affected healthcare outcomes. However, in LMICs, a paucity of effective policies was noted. Nevertheless, an emerging recognition of the potential of CPs to contribute to healthcare delivery is evident. The next section presents a brief description of the policy and practice of MUR by CPs in the developed countries and its impact on clinical, humanistic and economic outcomes in various chronic diseases.

MUR policies and practices in developed countries

The developed countries have taken a series of initiatives to reform policies which encourage inter-professional collaboration and expansion in the role of CPs in chronic diseases. It is regarded as a "global move" for an advanced care practice at community pharmacy beyond the traditional roles of dispensing and compounding to direct patient care.[17]

United States of America (USA)

The Medicare Prescription Drug, Improvement, and Modernisation Act, 2003, was the first effective move in the USA aimed at utilising drug expertise of CPs to optimise the use of medicine through a service which later came to be known as Medication Therapy Management (MTM).[18] In 2004, the working group of American Pharmacists Association (APhA) on MTM Services defined MTM as "a set of services that optimise therapeutic outcomes for individual patients". APhA and National Association of Chain Drug Stores Foundation collaboratively formulated the full code of conduct regarding MTM services and defined its five core components in a publication which received countrywide acceptance in pharmacy and medical circles. Later in 2008, the publication was updated with the title, "The Medication Therapy Management in Pharmacy Practice: Core Elements of an MTM Service Model".[18]

The historical Asheville Project, launched in 1997, was the first example where CPs were engaged to monitor appropriate use of medicines, impart education to patients, organise follow-ups and make timely referral, to target optimal therapeutic outcomes. Results of the study were significant for the outcomes, such as glycaemic control, quality of life, and knowledge about the diseases and medication. These findings also established monetary worth of bringing CPs' expertise in direct patient care, i.e., healthcare costs were reduced to range between $1,200 and $1,872 per patient per year.[19] Considering the value of the promising results, the Asheville Project was expanded to cover chronic diseases and it consistently demonstrated improvements in hyperlipidaemia, with 69% patients achieving the optimal level as against a baseline of 33%, hypertension, with 81% patients successfully maintaining their blood pressure in the optimal range, and in asthma.[19] Another prominent example was the Hickory Project which report on the sustainability of such outcomes over three years from 2007 to 2009 to confirm the advantages of involvement of CPs in the management of chronic diseases.[20-22] Similarly, Diabetes Ten City Challenge, a project which was delivered through CPs in 10 USA cities, reported significant improvement in diabetic patients' outcomes.[23]

A recent report to US Surgeon-General, "Improving patient and health system outcomes through advanced pharmacy practice", summarised evidence-based conclusion about the significant impact CPs' valuable contributions had made in MTM, adherence support and educational interventions to manage chronic diseases. It further went on to explain how such collaborative models of care can meet the challenges of health systems, like access to healthcare and medicine, high costs of therapy, overcoming barriers like GP workload, and shortage of providers, and ultimately contribute to overall improvement of community health. An estimated return on investment (ROI), an authentic measure of cost effectiveness of a service, for MTM was 12:1 and the report gave the credit to MTM/MUR performed by CPs which removed unnecessary or inappropriate medications, abridged hospital and emergency room (ER) admission and GP clinic visits.[24]

In the USA, formal agreements known as "collaborative practice agreement" exist which bind both GPs and CPs to run a collaborative practice. These agreements comprehensively, yet straightforwardly, define roles, set jurisdictions and outline modus operandi to manage chronic diseases collaboratively. Currently, in the USA, 45 states have authorised CPs' involvement in MTM to modify a drug therapy, and 38 states have regulations to initiate pharmacotherapy under collaborative practice agreements.[25]

United Kingdom (UK)

In the UK, almost 96% people live within 20-minute walking or a ride distance from a pharmacy. Pharmacies are functional for extended hours and may work 100 hours per week to cater to 438 million visits per year for queries related to health and medicines.[26] The UK, which includes England and Wales, has witnessed a gradual transformation in the roles of CPs for MUR, i.e., from an unorganised timeserver ad hoc review to a prescription review, which is a routine must-perform step during dispensing, to MUR, the first advanced CP service having been initiated in 2005, which checks meticulously all the medicine a patient is taking with the principal objective to improve patient compliance, to the latest clinical medication review which involves physical presence of patients with complete clinical history and notes. Scotland started a similar initiative in 2010, called the "Chronic Medication Review" (CMR).[27]

A white paper from the Department of Health, "Pharmacy in England: building on strengths, delivering the future", is considered a blueprint of the new models of pharmacy services which sets out the vision of policymakers in favour of expanding further the role of CPs in chronic disease management and public health.[28]

In the UK, the National Health Service (NHS) gave contracts to pharmacies which are private businesses. Under these contracts, pharmacies offer 3 main types of services, essential, advanced and enhanced, bounded by legislation which is known as the "National contractual framework for pharmacy".[29] Essential service deals with dispensing and repeat dispensing of medications and is an obligatory service for all pharmacies. Advanced services provide a comprehensive MUR to chronic patients. To avoid volume-driven services, emphasis is on a value-driven service, and that is why the number of maximum MURs per pharmacy per year is set to be 200 in the first year and 400 in the following year. CPs are reimbursed at the rate of £33.2 per MUR.[30] CPs record all interventions on a prescribe national MUR form, with multiple copies, and send them to the GP concerned with evidence-based recommendations. The enhanced services are of two types: clinical enhanced services, which cover chronic disease management, care home services and minor ailment services; and the public health-based enhanced services, mainly comprising weight management and smoking cessation. Another model which engaged CPs in public health activities was "Healthy Living Pharmacy" which not only promotes public health initiatives, but also focuses on early screening of chronic diseases at community pharmacies. This was successfully implemented in Portsmouth in 2009 and after its positive outcomes it was further expanded to other parts of the UK.[31]

New Medicine Service (NMS) in 2011 is the latest move in UK to strengthen the role of CPs. It has a unique focus which covers only chronic patients, promotes optimal use of medicine, reduces medicine waste, expedites early screening of chronic diseases, improves adherence and promotes self-management techniques through educational interventions. Currently, 85% pharmacies are providing this service. A study evaluated the extent of NMS implementation in community pharmacies to gauge the uptake of this service, and reported that the overall implementation process was successful. The service has been soaked in the daily routine of pharmacies.[32]

Canada

The document "Blueprint for pharmacy" explicitly describes the vision of Canada for advanced roles of CPs in the management of chronic diseases. The National Pharmacy Regulatory Association (NPRA) declared collaboration and team-work with GPs and other healthcare professionals as a professional competency for a pharmacist.[33] The Canadian Pharmacist Association (CPA) explained its vision for community pharmacy in a white paper, "Canadian pharmacy services framework 2011", which is a detailed protocol that sets modus operandi of how CPs would be utilised to rationalise the use of medicine across Canada. It has also provided a tiered structure of services provided to chronic patients similar to the UK. A recent publication from CPA provided evidence in support of therapeutic and cost-effectiveness of CPs' interventions in chronic diseases, notably in cardiovascular diseases, asthma and diabetes.[34]

The report, "Optimizing scopes of practice, new models of care for a new healthcare system", spotted the potential of CPs as a vast resource for public health activities, especially in chronic diseases.[35] Similarly, another report submitted to the Canadian Ministry of Health, titled "Broader pharmacy's plan for improving access to affordable healthcare", chartered five pharmacy-based initiatives to offer Canadians an affordable healthcare, treating minor ailments and vaccination at pharmacies, promoting cost-effective medications through the involvement of CPs, medicines and disease management in chronic cases with the aim of minimising the need of critical care, prevention of adverse drug reactions, and preparing pharmacies to respond to pandemics and emergencies. In 2016, CPs added value worth $12.5 billion to the Canadian healthcare system by avoiding ER and hospitalisation expenditure.[36]

Australia

Australia has demonstrated a sustained commitment to encouraging CP-delivered MUR in chronic disease

management. An array of services are offered by CPs under the ″5th Community pharmacy agreement″. There are two main types of MUR models under the supervision of CPs: those performed within the pharmacy setup, and those performed out of the pharmacy setup. MedsCheck, a general review of medicines for a patient taking 5 or more medicines, and Diabetes MedsCheck, a specific medicine check for diabetic population, are performed within the premises of pharmacy.[36] Some of the MUR models involve only an accredited CP who offers MUR services out of the pharmacyI. It includes Home Medication Review (HMR), also known as Domiciliary Medication Management Review (DMMR) and Residential Medication Management Review (RMMR). Both RMMR and HMR are reimbursed to CPs at the rate of $109.56 and $216.66, respectively.[37] The RMMR is older to HMR with only the difference being that it is applicable in residential care or medical home or aged care home setting only. It came into operation in 1997 under the ″2nd community pharmacy agreement″. It has two parts; one, the comprehensive review of the medicines, and, two, the focus on quality use of medicine plan. It can be performed by a GP and a CP in a collaborative fashion, known as ″collaborative review″, or can be performed solo by a CP, called the ″pharmacist only″ review and limited to 1 in 12 months. A comprehensive evaluation of RMMR was accomplished in 2010 and the report cited that RMMR was meeting expectations.[38]

Australia has endowed more than $663 million for the delivery of these services. It was the shining contribution of CPs which resulted in the creation of an image of pharmacy as the ″future health hub″ in Australia. Besides, Australia is also exploring potential new models or modifications in existing models to improve chronic disease management by CPs to the next level. This is depicted in the recent announcement of the Pharmaceutical Society of Australia, ″Call to Action on Chronic Diseases″, which has established an inseparable link between CPs and chronic patients.[38]

New Zealand (NZ)

″The Medicines New Zealand Strategy-2007″ reflected New Zealand's (NZ) vision to optimise the use of medicine in chronic diseases. This strategy highlighted salient steps towards cost-effective healthcare system where pharmacies work with district health boards through contracts. It demanded CPs to act as overseer of the inappropriate use of medicines, educate and encourage patients, and to have the capability to appraise outcomes of medicine use. This led to the formation of the first draft of ″Medicine management framework for the pharmacy profession″ by NZ district health board in 2007. It was later revised in collaboration with the Pharmaceutical Society of NZ to launch the ″Community pharmacy -term conditions services″. The document, ″Pharmacy 2015-20″, envisioned new models of care committed to utilising CPs' potential in chronic care.[39]

The ″New Zealand national pharmacist services framework-2014″ defined 5 core services, which, though varying in their scope of practice, were highly organised under two broad themes; one, medicine adherence services, which aimed at improving the use of medicines by the patients with MUR, pharmacy long-term conditions services, and two, medicine optimisation services which aimed at maximiing the therapeutic benefits through judicious decision-making based on pharmacotherapy principles including comprehensive medicine management, medicine therapy assessment, and community pharmacy anticoagulation management services. With the exception of comprehensive medicine management service, all services require CPs to get additional trainings and accreditations and they are reimbursed accordingly. For instance, MUR requires CPs to get accreditation of the Pharmacy Council of NZ against MUR standards.[40] Project Hawke's Bay District provided a clear evidence of the health outcomes in the form of improvement in the drug use and significant decline in the number of ER admissions. Another prominent example of effective utilisation of CPs was published from a project in Mid Central District Health Board where CPs were engaged to manage medicines used in asthma. Results showed improved adherence and increase in the knowledge of patients about the disease and drugs. Similarly, in the Canterbury region, a large number of pharmacies are running robust care delivery plans to offer patient-centred services through MUR services, and the number of MURs conducted during 2013 exceeded 5,000.[41]

Europe

Roughly 400,000 pharmacists work in 154,000 pharmacies to serve 46 million clients daily across Europe. Most pharmacies operate 24/7, and 98% Europeans can see a pharmacy within 30-minute walk.[42]

EuroPharm is an embodiment organisation working to meet the goals set by the World Health Organisation (WHO) for community pharmacy practice. EuroPharm also works closely with the International Pharmaceutical Federation (FIP) and the Pharmaceutical Care Network Europe (PCNE), which is a body of researchers in Europe working for the promotion of MUR, and has positively influenced the centuries old traditional role of CPs to move to the new paradigm of patient-oriented approach. It has primary focus on the provision of MUR services through

community pharmacies to manage the burden of chronic diseases and to promote population health. An expert panel appointed by the Council of Europe to suggest key indicators through which medication safety can be optimised has recommended this shift in the scope of community pharmacy practice which engaged CPs in a more active role in direct patient care. In Europe, there have been recent reforms in the practice of community

Table-3: Various attributes of Community Pharmacist led MUR practices in developed countries.

Country	MUR in community Pharmacy (Type/Since)		Patients Population	Patient's Interview	Guidelines for review	Patient clinical notes, lab test	Case dicussion with GP	Written follow-up plans	PG training Additional accredition needed	Payment
Bulgaria	Type I	1996	All	X	✓	X	X	X	X	X
	Type II		Chronic diseases	✓	✓	X	X	X	X	X
	Type III	-	-	-	-	-	-	-	-	-
Croatia	Type I	2005	All	✓	X	X	X	X	X	X
	Type II	2007	Chronic diseases	✓	X	✓	✓	✓	X	X
	Type III	2008	Chronic diseases	✓	✓	✓	✓	✓	X	X
Czech Republic	Type I	2005	Chronic diseases	✓	✓	✓	X	X	X	X
	Type II	-	Chronic diseases	✓	✓	✓	X	X	X	X
	Type III	-	-	-	-	-	-	-	-	-
Denmark	Type I	2001	All	X	X	X	X	X	X	X
	Type II	1998	Chronic diseases	✓	✓	✓	X	✓	✓	✓
	Type III	2000	Chronic diseases	✓	✓	✓	X	✓	✓	✓
Finland	Type I	-	All	X	X	X	X	X	X	X
	Type II	2001	CMR	✓	X	X	X	X	X	✓
	Type III	2005	Chronic diseases	✓	✓	✓	✓	✓	✓	✓
Hungary	Type I	1997	All	✓	X	X	X	X	X	X
	Type II	-	-	-	-	-	-	-	-	-
	Type III	-	-	-	-	-	-	-	-	-
Netherlands	Type I	1990	All	X	✓	✓	✓	✓	✓	X
	Type II	2010	Chronic diseases	X	✓	✓	✓	✓	✓	✓
	Type III	2010	Chronic diseases	✓	✓	✓	✓	✓	✓	✓
Sweden	Type I	2003	All	✓	✓	X	X	X	X	X
	Type II	2003	CMR	✓	✓	X	X	X	X	X
	Type III	-	Chronic diseases	✓	✓	✓	✓	✓	X	X
Switzerland	Type I	2001	CMR	✓	✓	X	✓	✓	X	✓
	Type II	2010	Chronic diseases	✓	✓	X	✓	✓	X	✓
	Type III			-	-	-	-	-	-	-
Norway	Type I	-	-	-	-	-	-	-	-	-
	Type II	2008	CMR	✓	✓	X	X	X	✓	✓
	Type III	-	-	-	-	-	-	-	-	-
Portugal	Type I	-	-	-	-	-	-	-	-	-
	Type II	2001	Chronic diseases & CMR	✓	✓	✓	✓	✓	✓	✓
	Type III			-	-	-	-	-	-	-
UK	Type I	-	-	-	-	-	-	-	-	-
	Type II	2005	Chronic diseases	✓	✓	X	✓	✓	X	✓
	Type III	-	-	-	-	-	-	-	-	-
Spain	Type I	-	-	-	-	-	-	-	-	-
	Type II	-	-	-	-	-	-	-	-	-
	Type III		Chronic diseases & CMR	✓	✓	✓	X	✓	✓	X
Belgium	Type I	-	-	-	-	-	-	-	-	-
	Type II	2013	Chronic diseases (only Asthma)	✓	✓	X	✓	✓	X	✓
	Type III	-	-	-	-	-	-	-	-	-
Germany	Type I	-	-	-	-	-	-	-	-	-
	Type II	2014	Chronic diseases (mainly diabetes)	✓	✓	X	X	✓	X	X
	Type III	-	-	-	-	-	-	-	-	-
	Type I	-	-	-	-	-	-	-	-	-
	Type II	2008	Chronic diseases	✓	✓	X	X	✓	✓	X
	Type III	-	-	-	-	-	-	-	-	-

CMR= Complex Medicine Regimen (polypharmacy), PG= postgraduate, GP= general practitioner, MUR= Medicine Use Review.

pharmacies but access to patients' clinical notes and labs tests is still restricted and not widely adopted. Nevertheless, European countries are increasingly involving pharmacies as a central place for public health activities. An important observation is the emergence of advanced level pharmacy services to cater to mainly the chronic patients. A large-scale survey across 25 countries in Europe effectively summarised the practice of MUR through community pharmacy. These countries were asked to mention about the types of MUR performed by CPs in their country. With the exception of France, Lativa and Iceland, 15/25 of European countries had at least one of the three types of MUR being practised in a community pharmacy setting, and 13 of these 15 countries had type-II MUR, while 9 had type-I MUR in community settings.[5] However, the advanced type-III level MUR was rare and was only practiced in 6 countries (Table 3). A brief description of the prevailing scenarios in various countries in Europe is in place.

Germany

German pharmacies and medical organisations have incentivised the CPs to lead MUR services for chronic disease management. An example is asthma management service offered at community pharmacy since 2003, and later implemented throughout the country based on its promising results in clinical outcomes, self-care and in patients' knowledge.[43] The Federal Union of German Associations of Pharmacists came up with a working paper, "Pharmacy 2030 – perspectives on provision of pharmacy services in Germany", shedding light on the possible future model of community pharmacy practice in Germany. This paper was widely accepted and served as the roadmap for the expanding roles of CPs in direct patient care. Since then, Germany has taken many serious initiatives to utilise its CP workforce in the best possible way following the USA model of MTM.[44] For instance, project ARzneiMittelINitiative Sachsen-Thuringen (ARMIN) engaged CPs to improve safety, effectiveness and cost-effectiveness of pharmacotherapy in chronic diseases. In the initial stages, the project was implemented in two German states, Saxony and Thuringia, for a period of 5 years from 2014 to 2019. The project focuses in three main areas; generic prescribing, use of an online medicine catalogue for GPs, and medication therapy management by a CP in the form of type-II MUR.[45] Similarly, project Arzneimitteltherapiesicherheit in Apotheken (ATHINA), which commissioned CPs for a structured MUR along with patient education and counselling, and many other projects are being executed from community pharmacies.[46]

Switzerland

In Switzerland, CPs are in the process of upgrading to a more patient-oriented role parallel to international developments. There are two models which may be compared with MUR elsewhere. "Prescription validation process" is somewhat like type-1 prescription review in the UK. However, counselling on adherence is not adopted extensively.[47] In 2010, following the footprints of UK model MUR, CP-led "polymedication check" was launched and CPs were reimbursed through insurance claims. This is first type of advanced service which is offered to patients who are using four or more medicines over three months' time, and generally cover elderly chronic disease patients in the Swiss population. Currently, Swiss pharmacies are dealing with 75% prescriptions which fall in this category, underlying the heavy responsibility of population health on CPs. During 2011, the recorded data of polymedication check cases performed by CPs were 2,534, which were increased by almost three times to 6,940 cases in 2014. Though implementation rate is slow and there are some barriers, the trend is encouraging.[48] Swiss initiatives are praiseworthy, "weekly pill organiser" and "polymedication check" are few examples of CPs leading medication management strategies. In addition to these services, CPs perform repeat dispensing in chronic diseases for a maximum of 12 months.[49]

Netherlands

Netherlands has expressed a consistent commitment to upgrade community pharmacy services after the promulgation of the Health Insurance Act-2006. Under this act, an advance level programme for CPs was introduced which required CPs to perform MUR for chronic patients. A prominent work by the Royal Dutch Pharmaceutical Society in the form of a white paper defined patient-oriented roles of CPs and attracted attention in this regard. Later, it was modified to formulate quality indicators for community pharmacy practice.[50] In the Netherlands, the Medication Monitoring and Optimisation programme was launched in 2013, which is comparable to MTM in the USA in scope and practice for chronic disease management. A large-scale study across the Netherlands demonstrated that CP-led MUR in chronic diseases had significant potential to detect drug-related problems (DRPs), and is thus a valuable source to optimise the therapy and ensure patient safety.[51]

Finland

Finland has extensive network of pharmacies mainly involved in counselling of medication during dispensing which is comparable to ad hoc reviews in the UK. In Finland, asthma and diabetes management were two services initially offered by CPs to public in 1997 and 2003, respectively. However, these services were not even comparable with MTM in the USA or New Medicine Service in the UK in terms of scope of practice. "Pharmacy Heart

Programme" was started in 2005 and covered cardiovascular diseases patients. In 2006, the government decided to utilise CPs to benefit older people with chronic diseases. The initiative also included detection of DRPs within community pharmacies.[52]

It is essential to mention that not all European countries have the same level of CP engagement. The practice of MUR has spread in Europe, and, over a period of less than a decade, many European countries have implemented one or the other form of MURs, especially for chronic diseases. The extent of reforms in health policies regarding the expansion of CPs' role across these countries highlight the readiness of CPs to join the patient care team, and, very importantly, the political will in favour of such reforms. Nevertheless, from a concrete policy point of view, on a comparative scale, the USA is behind Canada, Australia and the UK, who are now leading this concept of CP-led MUR in collaboration with GPs and have devised a staunch reimbursement system and proper tools to club pharmacy with primary care.[53]

Impact of CP-led MUR

A large number of studies have reported the impact of MUR provided by a pharmacist. However, it would be misleading to present the appraisal of these studies as an evidence of the CPs' contribution. This is because a large fraction of these studies either report hospital pharmacist contribution[54] or pharmacist in medical homes, or in a managed care settings[55] or integrated within GP settings[56] or mixed-setting studies which combine all the earlier mentioned settings[57] and hence, make the picture blurred for CPs. The studies which provided pure appraisal of CPs' contribution were limited and documented in recent literature only (Table 4).

MUR; policy and practice in low- and middle-income countries

In low- and middle-income countries (LMICs), the role of CPs related to MUR in chronic disease management is limited. This is especially true in Southeast Asia where in the last two decades, there has not been significant advancements in practice of community pharmacy in terms of quality and scope for CPs.[58]

In this region, pharmacy organisations are struggling to stretch and strengthen the roles of CPs in advanced patient care beyond dispensing, and many countries did have some initial success in implementing various health promotion activities to be based at community pharmacy, for instance, smoking cessation, weight management, diseases screening, sexual health, dealing with minor ailments and contraception.[59] However, the implementation of these roles and further extension to more advanced clinical roles in disease and medicine management are limited. There are various barriers which vary from country to country and are associated with this limited success; these include, prominently, less number of CPs, legal and political influence of physicians, lack of awareness and acceptance by the public and absence of an appropriate reimbursement system for the extended roles of CPs.[60]

A recent systematic review concluded that over the last two decades, there have been numerous attempts to expand the practice of community pharmacy which may improve health outcomes of an individual as well as population, but the pace of any such initiative remained slow and elusive, and thus, there is no strong evidence base to support and operationalise the untapped potential of CPs in patient care delivery as has been done by the developed countries An abridged form of data provided by reviews is available (Table 5).[59,61-63]

Discussion

The current narrative review compared current practices and policies regarding MUR by CPs to manage chronic diseases in developed world and LMICs. Medicine use process and delivery of healthcare is evolving around the globe from a single care provider to a collaborative care model, where CPs have much to contribute. "WHO Global Action Plan for the Non-Communicable diseases 2013-2020" also demands some basic policy reforms in healthcare system which may promote collaboration among various healthcare stakeholders.[64] MUR bridged the gap between two stakeholders, CPs and GPs, by proposing an opportunity of a strategic alliance of both professions based on collaboration and coexistence to benefit the patients. A healthcare system, if enabled and based on effective policies, may reciprocate the needs of people with chronic diseases. CPs could be valuable for the prescriber for an evidence-based decision-making in the choice of drug therapy and may bring alternative cost-effective solutions in the medication therapy.

In the developed countries, CPs' roles are expeditiously advancing to keep up momentum with the requirement of advanced healthcare system. Promising impact of CPs involvement in the management of chronic diseases was evident in high-income countries (HICs), especially for diabetes, asthma and hypertension. However, the situation in LMICs, which carry an overwhelming burden of chronic diseases, remains skimpy due to the absence of any concrete policy.

In LMICs, even today, CPs work in isolation from the rest of the primary care team and have never been engaged in patient care. In these countries, they have received a

Table-4: Various systematic reviews or overviews to appraise the impact of MUR or pharmaceutical care provided by Community Pharmacists in collaboration with General Practitioners.

Study (SR/MA/Overview of SRs)	Geographical & chronological coverage	Intervention/ Population/ Chronic diseases	Total studies added in the final synthesis	Comments & Conclusion
(Blenkinsopp & Hassey, 2005)[71] **(SR)**	International (1990-2003)	Medication review I Diabetes	7 interventional studies, (2 controlled, 4 open, 1 RCT on phone)	Main outcome measured were: control in diabetes in 3 studies, adherence to therapy in 2 studies, while DRPs and knowledge of the disease and drugs in one study each. The evidence was not strong for improvements in clinical outcome in diabetes, while knowledge of patients improved. Nevertheless, the number of interventional studies were few and lack of robust research designs at that time were the contributing factor towards the authors' conclusion.
(Roughead, Semple, & Vitry, 2005)[72] **(SR)**	International (1990-2003)	Medication review in many chronic diseases	22 RCT	CP's interventions as compared to a control were significantly positive for the clinical outcome in asthma, diabetes, blood pressure and cholesterol and improvement in optimal use of medicines. However, limited evidence on the improvement of quality of life and adherence were cited. Main problem in pooling the results statistically was the variability of outcomes end points which cannot be brought together in statistical terms.
(Van Wijk, Klungel, Heerdink, & De Boer, 2005)[73] **(SR)**	International (Incep-2003)	Interventions to improve adherence in all chronic diseases	18 studies (12 RCTs and 6 pre-post design)	Adherence was improved significantly in 8 studies, 2 studies did not show any difference, while 8 studies show no improvement. However, author related this non-improvement to high adherence values at baseline.
(Brown, Portlock, & Rutter, 2012)[74] **(SR)**	International (1990-2011)	Systematic reviews of all interventions of CPs in different chronic diseases	377 studies, including all types of research designs	Strength of evidence in each study was graded as per the standards defined by UK National Service Framework hierarchy of evidence. When chronic diseases were set in context of the strength of evidence, the evidence was strong for Diabetes and hypertension, need more research for asthma and heart failure, and was weak for COPD. In addition to chronic diseases, reviews also focused on other health promotion activities performed by CPs, and results were significant for smoking cessation (which is primarily linked with asthma as a precipitating factor).
(Blalock, Roberts, Lauffenburger, Thompson, & O 'connor, 2013)[75] **(SR)**	USA (2009-2011)	MTM in various chronic diseases	21 studies (12 RCT, 4 pre-post, 4 cohort, 1 non-randomized comparison)	Diabetes and hypertension were the focus of studies, for which results were favourable, where adherence, drug use, knowledge, self-care and quality of life were improved in more than 50% studies. However, evidence was limited for pulmonary functions improvements and lipid management.
(Jokanovic et al., 2016)[76] **(SR)**	Australia (2000-2015)	Medication review in all chronic diseases	9 controlled, 34 observational & uncontrolled, 11 interviews, 9 survey	The overall result indicated improvement in adherence to prescribed medication, successfully identified DRPs and was cost effective. However, lack of control group in majority studies slightly weakened the strength of the evidence.
(Ernieda Hatah et al., 2013) **(SR+MA)**	International (incep-2011)	Only fee for service medication reviews (MTM, MUR etc) in all chronic diseases	36 RCTs	Pooled results show, more than half of the studies confirmed that the service improved the adherence clinical outcomes in hypertension and lipid lowering drugs. However, no statistical significant difference was observed between the control and intervention group for hospitalization and mortality.

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Study (SR/MA/Overview of SRs)	Geographical & chronological coverage	Intervention/ Population/ Chronic diseases	Total studies added in the final synthesis	Comments & Conclusion
(Mossialos, Naci, & Courtin, 2013)[77] **(Overview of SR)**	International (2000-2012)	All chronic diseases	33 SRs	The overview of 33 SRs gave an insight into the effectiveness of CPs intervention on two broader aspects: a) effective, safe and appropriate use of medicines b) prevention and management of chronic diseases. The evidence is relatively stronger for chronic diseases management, while results remain inconclusive for the effectiveness of interventions to improve use of medications. Apart from this, author noted serious drawback in study selection in various SRs.
(Cheema, Sutcliffe, & Singer, 2014)[78] **(SR+MA)**	International (incep-2013)	Medication review for hypertension	16 RCTs	Meta-analysis of the studies indicated significant reduction in systolic and diastolic blood pressure with $p < 0.00001$.
(Jokanovic et al., 2016)[79] **(SR)**	International (incep-2015)	All evidence base interventions on hypertension and diabetes	16 RCT	All studies were consistently reported decrease in systolic BP and lowering of HbA1c.
(Jokanovic et al., 2016)[76] **Overview of SRs**	International (1995-2015)	Systematic reviews of all interventions of CPs	31 SR (24 moderate quality) (7 high quality)	The most favourable outcomes were recorded for Diabetes (78% of studies), then for blood pressure control (74% of studies). Medication adherence was improved in 56% studies. 35 % studies concluded CPs intervention in these diseases as cost effective. 12 SR quantified the outcomes through meta-analysis and results were promising for HbA1C, reduction in BP and cholesterol. However, reduction in the number of hospital admissions gave mixed findings and remained inconclusive.
(Gammie, Vogler, & Babar, 2017)[80] **(SR)**	International (2010-2015)	SR of economic impact	10 studies	Cost utility analysis was the most frequently used measure for the economic evaluation of CPs interventions, while no study used cost minimization analysis. Eight out of ten studies performed in community settings demonstrated that the interventions were cost effective and cost saving. Lack of quantification of results without any reason was a major lacking, author merely relied on narrative synthesis, that's why results remained elusive.
(Malet-Larrea et al., 2016)[81] **(SR)**	International (incep-2015)	SR of economic impact	13 RCT/C-RCT	Economic evaluations of RCTs or Clustered RCTs were pooled in the study. On quality scale, 7/13 studies were high, 3/13 medium, and 3/13 were of low quality. Estimated on effective and cost effectiveness scale, 4 studies concluded that CPs services were effective and cost effective than usual care, 2 studies calculated that CP's services are as effective as usual care but less costly, while,7 studies declared that CPs services are costlier. Effective and more costly than usual care. There was variability in terms of findings, but trend was towards the cost effectiveness of interventions. Authors also encouraged policy makers based on the available evidence to support pilot testing of these services.
(Mubarak, Hatah, Khan, & Zin, 2019)[82] **(SR+MA)**	International (incep- 2017)	Asthma	10 RCT/ CRCT	As a result of CP's interventions, the outcomes, such as asthma severity, asthma control, asthma symptoms, PEFR, SABA usage, hospital visit, adherence, and quality of life demonstrated a small effect size (ES) (d?0.2), while ED visit, and asthma knowledge witnessed medium effect sizes (d?0.5). In addition to that, inhalation technique yielded large ES (d?0.8). The outcomes such as FEV, corticosteroids usage, and preventer-to-reliever ratio, did not hold significant ES ($d<0.2$) and, thus, remained inconclusive.

CP= community pharmacist, GP= general practitioner, CRCT= cluster randomized controlled trials, RCT= randomized controlled trials, SR= systematic reviews, MA= meta-analysis, COPD= Chronic Obstructive Pulmonary Disease, UK= United Kingdom, USA= United states of America, MTM= medication therapy management, MUR= Medicine Use Review, BP= blood pressure, HbA1c= hemoglobin A1c, DRP= dug related problem, PEFR= Peal expiratory flow rate, SABA= short-acting beta agonists, FEV= forced expiratory volume, ES= effect size, ED= emergency department.

Table-5: Community Pharmacist and General Practitioner collaboration in East-Asia.

Country	Medication review OR Traditional Counselling (TC)	Legislature Support	Guideline	Dispensing Separation	Chronic Disease Services	Reimbursement	Comments & Conclusion
China	TC	✖	✖	✖	✖	✖	Health system reforms 2009 have placed CPs in more spotlight. However, role of CPs has not been much advanced in-patient care but evolving. Shortage of CPs and lack of reimbursement are barriers to expand the scope of CP practice beyond TC. Furthermore, CPs need more clinical skills to adopt the changes necessary to offer MUR type of services.[83,84]
Taiwan	TC	✖	✖	✔	✖	✖	Limited number of prescription received at community pharmacy, which itself is in developing stages.[85,86] However, there is a kind of re-nascence since 2009, when CPs were involved in Home Care (like HMR in Australia). The service demonstrated economic value (1:1.4), and thus now became inseparable part of pharmacy practice. Furthermore, in 2015, CPs in Taiwan started diabetes management in collaboration with GPs.[36]
Singapore	TC	✖	✖	✖	✔	✖	CP are taking part in many health promotion activities, like smoking cessation, weight management, etc. They are successful in developing practice guideline for minor ailments. Community Pharmacy Health Champion Program a local initiative, has some potential to grow into a full fledge medication management services for chronic diseases. However, lack of legislature support diminishes the spread. Medication reviews, home visits, and chronic disease management are in the next steps in pipeline.[87]
Korea	TC	✖	✖	✔	✖	✖	The situation is very similar as other countries in the region. Lack of legislature support for medication reviews made the service limited to traditional counselling. South Korea is leading in a sense it has enacted dispensing separation, which is decisive factor when it comes to extension in roles of CPs in patient care.[88-90] It is South Korea, where dispensing separation has been implemented, since July 1st, 2001. CPs are involved now in prescription handling, but no specific chronic diseases related service is offered. However, CPs are aware of their emerging roles in patient care.[91]
Japan	TC		✖	✔	✖	✖	With dispensing separation in practice, CPs role is expanding. However, role has not been grown beyond dispensing. However, generic substitution is operational in pharmacies. In terms of skills of CPs, more training is required. However, a recent study acknowledged the effectiveness of CP performed MUR as a beneficial tool to detect any DRP.[92-94]
Thailand	TC	✖	✖	✔	✖	✖	The introduction of the concept of quality drug store has resulted in translatable quality indictor which are being practiced by CPs in Thailand. CPs are involved in counselling and medicine checks but not that level which may be compared with a developed country.[95,96]
Hong Kong	TC	✖	✖	✔	✖	✖	Currently, the role is expanding in terms of CP utilization in various health promotion activities. Hong Kong is in planning phase for medicine use review services in management of chronic diseases.[97,98] The Hong Kong Medication Check Up and Clean Up service provided by a CP to prevent drug wastage and optimize use of medications in general public could be considered the first step towards utilization of CPs in this regards.[36]

CP= community pharmacist, GP= general practitioner, MUR= Medicine Use Review, UHC= Universal Health Coverage, TC= traditional counselling, DRP= drug related problem.

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Country	Medication review OR Traditional Counselling (TC)	Legislature Support	Guideline	Dispensing Separation	Chronic Disease Services	Reimbursement	Comments & Conclusion
Indonesia	TC	✖	✔	✔	✔	✖	Although, there exist separation of dispensing and prescribing, to some extent, CPs are delivering pharmaceutical care services in community to chronic diseases. However, it has faced many barriers, including CPs lack of training and thus delivery remain suboptimal. Introduction of standards for Pharmaceutical Care in Community Pharmacies, 2006, was the initiations of an opportunity for CP to offer their contribution in chronic disease management. Although, there is limited data on the evaluation of such services, but at least the process has started which involves prescription review, monitoring of medication use. Government has started implementing Universal Health Coverage (UHC), since 2014 in a stepwise approach and intends to complete by 2019. UHC will definitely enhance the collaboration level between CP & GP.[99,100]
Philippines	TC	✖	✔	✔	✖	✖	Although, dispensing separation is in operation, however, the practice is mainly dispensing with traditional counselling. Nonetheless, in hospitals pharmacist offer range of clinical services. Philippian government is taking some serious initiative to enhance CPs' offered direct patient care, including lobbing for the passing of New Pharmacy Law to extend the role of CPs. Similarly, formulation of National Antimicrobial Use Guidelines and vaccination by CPs are some steps worth mentioning.[101,102]
Malaysia	TC	✖	✔	✖	✖	✖	Pharmacist in hospitals have quite good service structure, however, community pharmacy is neglected. CPs are still struggling to convince ministry to implement Dispensing Separation. However, recent studies have documented the healthcare stakeholders' consensus on CP-GP collaborative medicine management model in chronic diseases.[70]
Pakistan	TC	✖	✖	✔	✖	✖	No stringent policies or guidelines exist for the services such as MUR. Quality of counselling is poor and rampant sale of drugs which require prescriptions is evident.[103] Experts believe that CP could be a potential resource to rationalize the drug use, if utilized under a legal framework can benefit the ageing population.[104] There is need of further research pertaining to pharmaceutical policy and practice pertaining to community pharmacy.
India	TC	✖	✖	–	✖	✖	The main role of CP is still restricted to merely selling of medicines. However, in the wake of international developments, without any legal frame work, CP do offer certain services for instance weight management or treatment of minor ailments.[105,106]

limited scope of practice which mainly revolves around traditional roles of dispensing and compounding with a lean patchy role in direct patient care. A recent study found short GP consultation time in Southeast Asian countries, representing almost 50% population of the globe, from 5 minutes to as low as 47 seconds in Bangladesh. The study established a correlation of shorter GP consultation time with decline in the quality of necessary monitoring of drug therapy, patient counselling and education from the GPs[65] and in fact implied the need of MUR by a qualified healthcare professional to optimise the therapeutic goals.

The other side of the argument is the huge population in these countries. Involving CPs in chronic disease management would decrease the burden on GPs, but it requires specialist CPs for specific chronic diseases. Although many countries have upgraded the pharmacy curriculum to Pharm D degree, to give a clinical tilt, but experts believe the current Pharm-D or Bachelor of Studies (BS) Pharmacy curricula in Southeast Asia do not equip pharmacy graduates to keep pace with international developments.[66]

LMICs must rethink the protocols they used to manage chronic diseases. In these countries, involving CPs in chronic care through a policy change is an intricate process which not only requires political will but also extensive research to better understand various stakeholders' perspectives and their level of agreement with each other on the issues which may hinder the successful implementation of any model of care through community pharmacy for chronic disease management. The lessons learnt from developed countries may be used as a guide for stakeholders in LMICs to frame the health policy based on country-specific scenarios.[67] It is imperative to consider barriers in country-specific context and experts should come forward with a policy which is plausible and acceptable for various stakeholders in a specific country. This is because healthcare professionals who should work together as a team to benefit the patient are always in a mode of turf war. GPs believe it would be like handing over patients to CPs. Pharmacists are not the "medication police" or there to keep a check on the prescribing habits of GPs. The aim is to make patients better understand their medicines to maximise the therapeutic outcomes and keeping adverse effect at minimum. Healthcare is teamwork, and in a team, different players come up with skills which may appear different but actually are complimentary. It is just like a football team full of quarterbacks would not get anything done.

A recent systematic review found two most effective implementation strategies for MUR; one, "Train and educate stakeholders", and, two, "engage consumer".[68] A practical attempt to develop consensus among conflicting healthcare stakeholders on various reforms to bring CPs in chronic care management can be cited from Abu Dhabi[69] and Malaysia.[70] It is believed that the way forward to a paradigm shift in any country must involve consensus-building methods to bring relevant stakeholders on the same page.

Conclusion

Addition of CP-led MUR in chronic disease management particularly holds importance as a potential reform in healthcare system. These policy reforms may differ in terms of scope of practice, but should have one common objective to procure benefits from the expertise of CPs. Numerous studies are evident of this gradual paradigm transformation of CPs' role and fading image of being retailer or shopkeeper to healthcare professional, the "drug therapy manager" with an expanded focus on medicine management, MUR, adherence support, and economical use of medications in the community. Healthcare reforms are shared globally and tested for efficacy in different countries and its modalities change from country to country, but every country needs a smarter care which combines cost-effectiveness and efficacy. LMICs have abandoned the role of CPs, while the world has gone beyond dispensing separation.

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