



Electronic Health Records, Electronic Prescribing and Medication Errors: A Systematic Review of Literature, 2000-2014

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Authors' contributions

This work was carried out in collaboration between all authors. Authors NAQ and DSAD developed the concept and designed the study. Authors NAQ, DSAD, ANSA and IAAZ wrote the protocol and discussed with all authors. Authors NAQ, AMAB and HGK wrote the first draft of the manuscript. Authors NAQ, DSAD, IAAZ and ANSA managed the literature searches and analyses of the study data. Authors NAQ and HGK revised this paper a number of times. All authors read and approved the final manuscript.

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ABSTRACT

Background: The electronic prescribing system, either standalone or embedded in the electronic health record, is a powerful tool in the hands of healthcare providers, as it reduces half of medication errors caused by handwritten prescribing.

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Objective: This article synthesizes the international literature on electronic health records (EHRs), e-prescribing (EP) and medication errors (MEs) and provides a platform to World Health Organization Eastern Mediterranean Region (WHO-EMR) countries for implementing EHRs and EP in healthcare system.

Methods: Computer searches of PubMed, MEDLINE, Quertle®, Google Scholar, Web Knowledge and International Pharmacy Abstract databases were conducted for the years 2000–2014 using several single- and combined-keyword strategies, with 184 articles retained for evaluation.

Results: Although e-prescribing integrated with EHR reduces medication errors at all healthcare levels, decreases morbidity and mortality, enhances patient and healthcare provider satisfaction by reducing costs and improving quality of life, it produces different types of medication errors at various stages of the prescription process. An EHR with EP that has a clinical decision support system (CDSS), dose-limit range, drug–drug interaction alert protocols, and formulary decision support helps to improve EP and ensures greater patient safety and other multiple applications.

Conclusion: EHRs with EP systems should be implemented in healthcare systems for the sake of better quality healthcare and patient safety throughout the WHO-EMR countries especially in the Kingdom of Saudi Arabia. Evidently there is limited data in these countries and hence further studies are needed to assess impact of EHRs and EP system (EPSs) on medication errors, quality of healthcare, patient safety and outcome, morbidity and mortality rates, patients' and healthcare providers' acceptance, and especially its cost-effectiveness.

Keywords: e-prescribing system; electronic health records; clinical decision support systems; dose-limit range; drug–drug interactions; medication errors; Saudi Arabia.

ABBREVIATIONS

WHO-EMR = World Health Organization Eastern Mediterranean Region; EP = Electronic Prescribing; EHRs = Electronic Health Records; EMRs = Electronic Medical Records; EPSs= Electronic Prescribing Systems; MEs = Medication Errors; CDSSs= Clinical Decision Support Systems; CPOE = Computerized Physician Order Entry; NOE = Nurse Order Entry; DDI =Drug-Drug Interaction; PHC = Primary Health Care; HIT= Health Information Technology; T2DM = type 2 Diabetes Mellitus; LDL-C= Low-Density Lipoprotein Cholesterol; HBV = Hepatitis B Virus; ACEI/ARB = Angiotensin Converting Enzyme Inhibitors/Angiotensin Receptor Blockers; eMMS= Electronic Medication Management System; CHAID = Chi-squared Automatic Interaction Detection; IPA = International Pharmacy Abstracts; WOK = Web of Knowledge; RCTs = Randomized Clinical Trials; ACA = Affordable Care Act, NPS = National Patients Summary; ADEs/Rs = Adverse Drug Events/Reactions; DRPs = Drug – Related Problems; MOLs = Medication Order Lines; FDS = Formulary Decision Support; PCTs = Primary Care Trusts; VA = Veterans Affairs; EPSR2 = EPS release 2; ERs = Electronic Rules; PCPs= Primary Care Physicians; eMARs = Electronic Medication Administration Records; BCMA = Bar-code-assisted Medication Administration; KSMC = King Saud Medical City; NMs = Near Misses.

1. INTRODUCTION

Electronic prescribing (EP) is an integral part of e-Health, which is the use of information and communication technology in healthcare systems. EP does not stand alone in hospitals and healthcare facilities. In fact it is more likely to fail if it occurs in isolation from its overall environment. Based on the reports of Institute of Medicine and many other studies, both the United States and the European Union place emphasis on the greater use of health informatics and EP in all healthcare settings throughout the world [1]. There is increasing evidence that EP is associated with reduced medication errors (MEs), especially in terms of

dosage form and omission and commission types of errors in ambulatory and inpatient settings in all specialties. Overall, EP is associated with decreased morbidity and mortality, enhanced quality of healthcare services with less costs, better administrative control, improved working efficiency, and enhanced satisfaction both of healthcare providers and consumers [2-5]. Furthermore in a systematic review involving 47 sources on e-prescribing, Porterfield and associates suggested that medication errors are substantially reduced (70%) and cost savings attributed to patients outcomes and visits are estimated to be between \$140 billion and \$240 billion over a decade. Barriers to e-prescribing implementation are cost,

lack of provider support, patient privacy, system errors, and legal issues [6]. According to another review, paper-based prescription errors are substantially improved by EPS [7].

1.1 Rationale and Scope

The WHO Eastern Mediterranean Region (WHO EMR) is far behind when it comes to e-prescribing and the use of electronic health records. Therefore, we synthesize here the international literature on the use of electronic prescribing across healthcare areas. The scope of this paper is much larger because it reviews electronic prescribing across all ages and healthcare specialties.

1.2 Objective

This systematic review has the following objectives; 1) to synthesize international data on EP, EHRs and EMRs; 2) to identify new types of MEs facilitated by EP; 3) to identify strategies for preventing MEs across all healthcare settings, and 4) the uses of EHRs integrated with EPS.

1.3 Research Questions

This review has the following questions; 1) what are the pros and cons of electronic prescribing? 2) Why and how new types of MEs are caused by EP? 3) What are the strategies for preventing MEs in healthcare systems? and 4) what are the uses of EHRs, EMRs and EP?

2. METHODS AND MATERIALS

2.1 Search Strategy

Computer searches of the largest online databases – PubMed, MEDLINE, International Pharmacy Abstracts [IPA], Google Scholar, Web of Knowledge [WOK], and Quertle® – were conducted and limited to the years 2000–2014 in order to focus on the recent studies. The key search terms were electronic health record, electronic medical record, e-prescribing, medication errors, e-prescriptions, e-prescribing system, computerized physician order entry, and nurse order entry with combination of 'AND/OR' Boolean operators'. Boolean Operators are simple words such as AND, OR, NOT or AND NOT and they are used as conjunctions to combine or exclude keywords in a search. Beside more focused and productive results, they save time and effort by eliminating

inappropriate hits that must be scanned before discarding. These keywords were combined with hospitals, primary health care, in- and out-patient care, and academic centers, children, adults and elderly and medicine and surgical settings. Retrieved using this method were more than 6,150 articles. Many articles were excluded including articles without abstracts (n=86), papers not published in English language (n=105), full articles not available (n=253), duplication of articles across searches (n=3,326), and many papers unrelated to the topic under consideration (n=2,216). Only 164 papers were retained for further review. As database searches do not always reveal all of the pertinent literature, hand searches of relevant journals complemented by cross-references of selected articles were also made [n=14]. Thus, the authors selected 178 articles which included open label clinical trials, randomized controlled trials, systematic reviews and meta-analyses, all targeting the use of electronic prescribing systems, either standalone systems or those embedded in electronic health record (PRISMA chart 1).

Three investigators (NAQ, DSD, and AMB) independently reviewed the titles and abstracts of all retrieved articles to identify eligible studies. The investigators used pre-standardized data abstraction forms to extract data from relevant articles. All authors resolved differences by consensus and agreed on the inclusion of articles for this paper. These studies met below inclusion and exclusion criteria. Letters/correspondences to the editor were not included. We also searched Middle Eastern literature especially WHO Eastern Mediterranean Regional Office Health Journal, Saudi Medical J, Annals of Saudi Medicine, and Saudi Pharmaceutical Journal and Oman Medical J using the same search strategy and found several studies that focused on non-electronic medication prescribing (N=17). We did not include these studies in this paper because these studies are summarized elsewhere [8]. However, a few studies on electronic prescribing (n=6) were included to provide a local perspective on e-prescribing. Total studies in this review were 184.

2.2 Criteria for Inclusion and Exclusion

Criteria for selecting eligible studies on EHRs, e-prescribing and medication errors were as follows: 1) cross-sectional surveys and studies with quantitative, qualitative and mix type

methods including open label clinical trials, RCTs, systematic reviews and meta-analyses 2) studies that recruited physicians, managers, paramedical staff and others including leaders and patients as participants and assessed the outcome of EPSs, 3) studies that explored perceptions of participants about EHRs, EMRs,, CPOE, alerts, EP and MEs 4) research that defined EHRs, EP and MEs, 5) studies published in English language, 6) studies met the quality control measures given below (score 8 or > 8), and 7) those studies which explored attitudes and behaviors of participants that influence adoption of EHRs and EP system (EPS). Studies not meeting these inclusion criteria were excluded.

2.3 Quality Assessment

A quality assessment tool (Table 1) was used for study scientific rigor. This rating process was carried out independently by 4 of the authors (NAQ, AMB, DSD and IAZ). Interrater reliability was 80%, which was acceptable. Any disagreements about ratings were discussed between all authors until consensus was reached. A score of 8 or more qualifies a study to be of good quality.

3. RESULTS

3.1 Pros and Cons of EP

In a UK qualitative research of Hospital physicians' and pharmacists perceptions and predictors of satisfaction from EPS, pharmacists were more satisfied with EPS than physicians, and satisfaction predictors about its efficiency were stronger than predictors of quality of patient care [9]. Electronic prescribing and the electronic health record are founded on well-defined standards, principles and working mechanisms and perform many functions with many advantages over paper-written prescriptions [10]. However, effective implementation of EPS needs planning and preparation for effectively integrating EP into clinical work [11]. Researchers have suggested a number of strategies for the development and implementation of computerized physician order entry (CPOE) for chemotherapy in pediatric cancer settings, including that CPOE system must be safe, cost-effective and efficient; the extensive use of electronic order sets with advanced functionality; formal process redesign and system analysis; automated clinical decision

support system (CDSS); and a phased implementation approach. With careful planning and adequate resources, researchers concluded that CPOE for chemotherapy can be safely implemented [12]. In another study in children that took place in a tertiary care teaching hospital, EP reduced dosing errors, a common problem in pediatric population and possibly its severity, however larger studies are required to assess the severity of these errors and in different settings [13]. Risk management analysis in children hospital settings suggested the following strategies for reducing drug administration errors in infants: e-prescribing, dispensing and administering system, centralized drug preparations, and automated drugs cabinets [14]. There is an additional need to evaluate the performance of EPS and its impact on the occurrence of medication errors and other unwanted consequences including increased use of multiple pharmacies by patients after EP implementation [15]. One study reported that EPS has no significant impact on total medication errors together with increased callback rate, and required training of staff that was often associated with high costs, redesigning staff workflow, and regulatory bottlenecks [16]. Another study in a primary care setting reported that EP takes longer than hand prescribing and also takes more time at point of care than EP in offices and work stations [17]. We have further reviewed these perspectives including challenges and barriers for implementing electronic prescribing system [8]. Some researchers identified procurement challenges including lack of opportunity for interactions between customers and potential suppliers and additional components of EPS including timescale and deliverability and risk analysis and management through qualitatively analyzing the perceptions of several stakeholders for business case development for EPS [18]. In another qualitative study, Cresswell and colleagues reported that the maximum chances of realizing benefits of EP in NHS hospitals was associated with increased guidance for implementation, system choice and standards, as well as increased financial resources [19]. One qualitative study in UK primary care trusts (PCT) reported that beside the seven main reasons of prescribing and monitoring errors, computer-related issues associated with selecting the wrong drugs from electronic pick-lists and overriding alerts were possible causes of prescribing errors [20].

PRISMA Chart 1:

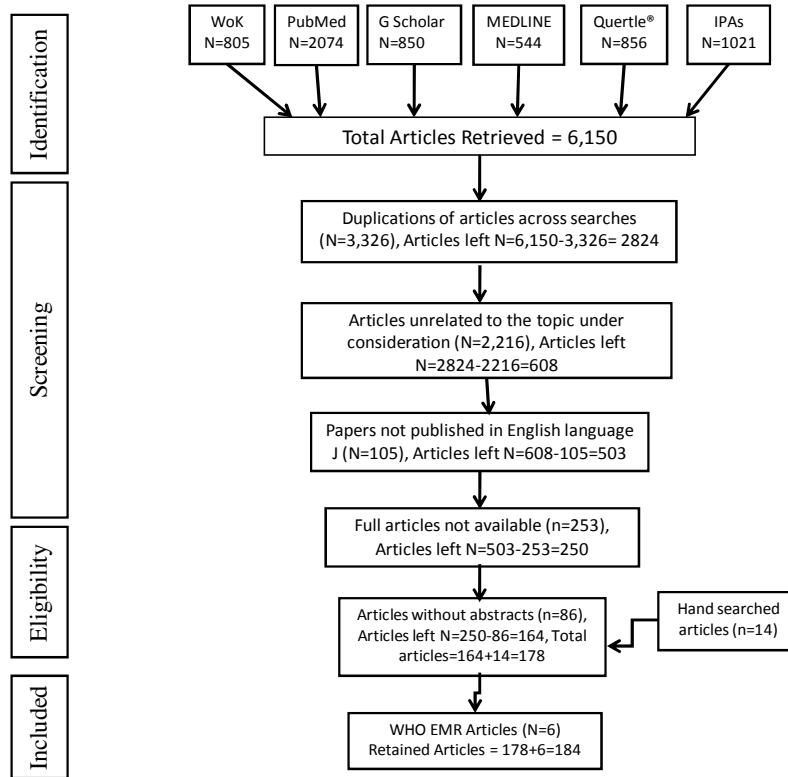


Chart 1. PRISMA Chart with study selection steps

Table 1. Quality assessment tool

Quality assessment for eligible studies	Yes	No	Neutral
1. Did the study address a clearly focused question (s)?			
2. Was the research method appropriate for answering the research question (s)?			
3. Was the method for selecting study participants clearly described?			
4. Could the sampling technique introduce bias?			
5. Was the recruited sample representative of the population?			
6. Did the sample size reflect pre-study consideration of statistical power?			
7. Was a satisfactory response rate achieved?			
8. Were the measurement tools likely to be reliable and valid?			
9. Was the statistical significance assessed by using appropriate tests?			
10. Were the data analyzed for calculating 95% confidence intervals?			
11. Could there be confounding factors not considered in data analysis?			
12. Can the results be applied to a respective health organization/setting?			

3.2 Electronic Health Records

An EHR is an electronic version of a patient's medical history. It is maintained by the healthcare provider over time, and may include all of the key administrative clinical data relevant to that person's care under a particular healthcare provider. The data may include

sociodemographics, key symptoms, diagnosis, progress notes, problems and incidences, prescribed medications, record of vital signs, past medical history, family history of any disease, immunizations, laboratory results and radiology reports. The EHR automates access to information and streamlines the clinician's workflow in a cost effective manner. The EHR

also supports other healthcare-related activities directly or indirectly through various interfaces, including evidence-based decision support, quality management, and outcomes reporting. EHRs tend to strengthen the relationship between patients and clinicians and other stakeholders. The EHR improves patient care by: 1) reducing the incidence of medical/medication errors, and 2) making the health information available, reducing duplication of tests, and reducing delays in treatment. The electronic health records have benefits for patients and physicians and other stakeholders including drug makers, insurance companies, and government agencies that could mine data to improve treatment with cost effectiveness and also use it later for training and research purposes. Through patients' portals, patients also have access to their data and follow-up that can help physicians to make better decisions with patient safety enhanced. It was demonstrated in a study that when doctors switched from paper to digital records, their diabetic patients made 5.5 percent fewer trips to the emergency room and were hospitalized 5.3 percent fewer times. These modest gains added up to a savings of \$158,478 for every 1,000 patients. The EHR is an integrated system that allows everything to work better and in a more cost-effective way [21]. In a study using discrete-event simulation model in ambulatory setting, Zhou and colleagues reported that the impact of using health information technology (HIT) on clinical and nonclinical staff work efficiency varies, however, overall it improves time efficiency more for administrators than for physicians and nurses [22]. In a focused review, Odukoya and Chui suggested that human factors engineering concepts need to be utilized for studying e-prescribing safety in pharmacies and primary care settings to identify safety problems and possible mechanisms for improvement [23]. The certified EHRs streamline several goals of the USA Affordable Care Act (ACA) of 2010 including reducing hospital readmissions and encouraging the development of more accountable doctors, hospitals, and other professionals involved in the care of healthcare consumers. In addition, extraction of data by automatic and semiautomatic methods about treatments such as anti-TNF infliximab administered to patients in hospital settings makes sense in the form of demographic, clinical, diagnoses, and dosages for treatment with medication [24]. Furthermore, another application of EHR data in pharmaco-vigilance studies is to identify potentially risky treatments

such as citalopram and other selective serotonin reuptake inhibitors (SSRIs) used in populations with depression that cause cardiovascular effects such as prolonging corrected QT interval (QTC) and other cardiac arrhythmias [25]. Moreover, health information technology in terms of EHRs and EPSs will require practice changes, training and redesigning of work processes in order to smoothly exchange the potential information across multiple interfaces [26].

Electronic medical records are used for clinical services mainly for the diagnosis and treatment of the patients, whereas EHRs have wider scope with interoperability and automation and also enhance patient's engagement in decision making process. Though e-prescriptions are more applicable to EMRs, e-prescribing system is also integrated with EHRs. EPS alone with multiple support systems like CDSS can perform treatment-related activities including guiding healthcare providers correctly write prescriptions and transmitting to hospital in-and out-patient and community pharmacies. Several researchers have described e-prescribing and terminologies together with EMR's potential benefits such as increased patient safety and efficiency and also drawbacks such as newly introduced medication errors and diminished workflow efficiency [8,27]. Different EPSs have large heterogeneity among functionalities and performances. To address this issue, Marceglia and colleagues developed an updated comprehensive model for the EP process, which is able to compare current systems and support the design of new systems to sustain the EP process at the national level. Six phases of EP process were identified: assignment, transmission, dispensing, administration, monitoring, and analysis decision. Each phase creates digital data for use in the next phase. Consequently, EP benefits impact governance, drug surveillance, and quality of care at the individual, territorial, and governmental levels. The study concluded that model-based implementation of each phase is associated with positive impact on quality of patient care, the access, and the effectiveness including its possible cost-effectiveness [28]. Some studies described two discrete-event simulation models, one for the current handwritten prescribing system and one for a proposed e-prescribing system, to compare the performance of these two systems. Ghany and associates concluded that a more appropriate approach to modeling both the handwritten and EPSs would be to use a complex adaptive systems approach using agent-based modeling

or systems-based modeling [29]. In a qualitative study involving 9 focus groups of doctors in a teaching hospital and primary health care center of same geographical area, a shared EMR was found to improve communication about prescribed medication between primary care and secondary care settings. The study identified differences between “access to data and information” and “access to knowledge” in a shared EMR; however, they emphasized that an increased availability of data should not be at the expense of a reduced availability of knowledge [30]. EHR embedded with EP adopters should meet e-prescribing requirements, or else they may pay the price [31].

3.3 Electronic Prescribing Studies

There is more literature on EP from the Western world than from the Eastern. Some of the studies are discussed below and summarized in Table 2.

3.4 EP Studies in PHC and Community

A study of EP in four adult primary health care (PHC) practices screened 1879 prescriptions from 1202 patients and completed 661 surveys assessing several elements of the process as well as the potential impact of prescribing errors. According to this study, errors occurred in 7.6% of prescriptions. Of these, 3% could have harmed patients. This finding indicates that more advanced EPSs with dose and frequency checking are needed to prevent MEs [39]. In a study of community based office practices where MEs occur more frequently, Kaushal and colleagues reported e-prescribing considerable reduced medication errors compared to baseline paper written errors and illegibility errors of handwritten prescriptions were completely removed, thus stand-alone e-prescribing system improves medication safety in ambulatory care [87]. In a systematic review that included 19 eligible observational studies on second-generation eRx technologies and focused on networking various stakeholders communicating electronically found that there is little empirical data demonstrating benefits to second-generation electronic prescription (eRx) technologies. According to this review, more studies are required that measure the impacts of second-generation technologies using empirical data and conducted in the context of actual use [88]. Swedish researchers conducted a web-based survey aimed at evaluating physicians' attitudes to EP [61]. A majority of the

respondents reported positive opinions regarding multiple aspects of EHR systems and EP. Respondents indicated that these systems were easy to use for the prescribing of drugs and provided better services, and regarded e-prescriptions to be time saving and safer than handwritten prescriptions. Based on perceived weaknesses of EHR systems, physicians suggested a number of improvements, including that drug choices be simplified, but were generally satisfied with both specific EHR systems and EP. According to one study, the gaps needing to be bridged in adopting e-prescribing in primary healthcare related to physician, policy and technology levels [89].

In a qualitative study using a modified Delphi process with twelve expert group members, Sweidan and associates explored the impact of EPS features (a list of 114) on the four domains of patient safety, quality of care, usefulness to clinicians, and usefulness to patients [66]. The expert group identified features related to the recording and use of patient data, the medication selection process, prescribing decision support, monitoring drug therapy and clinical reports that were likely to have a high positive impact, medium-level positive impact, low-level positive impact, or negative impact across the four domains. The study concluded by defining the features of EP systems that are expected to support safety and quality, especially in relation to prescribing and use of medicines in general practice. The features could be used to develop software standards and adapted, if necessary, for use in other settings and countries [66]. In an internet-based survey, 83% of PCPs reported being satisfied with EP and 22% of physicians indicated that they had started then stopped EP; however, most of these either had resumed or intended to resume EP in the near future [76]. More than half of the respondents reported experiencing problems with EP software.

In a study with controlled design, Moniz et al. [90] reported that CPOE generating e-prescription transmission to community pharmacies reduced 50% risk of dispensing errors compared to when printed prescriptions were given to patients to take to community pharmacies. However, a study using observational and think aloud protocols with sociotechnical framework recommended that retail pharmacies need e-prescribing standards and sociotechnical framework, which they thought was useful in understanding the interface between e-prescribing technology and the pharmacist and pharmacy technician [88].

Table 2. Summary of electronic prescribing (EP) studies

Study	Study theme, setting and areas	Study results and comments
Odukoya et al. USA [32]	To explore e-prescribing errors in community pharmacies, their potential consequences, and the factors underlying e-prescribing errors. Data collection involved performing 45 total hours of direct observation in five pharmacies, in addition to interviews with 20 study participants.	Several types of MEs involving 5% of e-prescriptions were reported. Multiple drug classes including anti-infective agents were found with MEs. Potential consequences of MEs due to technology design issues and incorrect entries were wrong drug type or dose, poor disease management, increased costs, and staff and patient frustration.
Ahmed et al. UK [33]	Cross-sectional survey of pharmacists about EP and use of multiple EPSs in acute hospitals, UK.	UK government encourages EP and EPSs, although many acute hospitals use multiple EPS within the same hospital that could create challenges for staff training and patient safety.
Gagnon et al. Canada [34]	A systematic review of 34 criteria-based publications, including 28 individual studies for identifying users' perceptions of barriers or facilitators of EP in PHC.	This review found 594 elements as barriers or facilitators to EP implementation. Most participants perceived that EP was facilitated by multiple factors including design and technical concerns. The findings of this review could help decision makers to design implementation approaches of EP in PHC.
Teich et al. USA [10]	Evaluation - CPOE system by time series analysis	Decreased MEs and fewer non-intercepted serious MEs; CPOE supported by CDSSs decrease in MEs
Nanji et USA [35]	Qualitative study to identify and characterize the unrealized potential and consequences of EP on pharmacy workflow in an outpatient pharmacy.	Themes and subthemes related to weaknesses of EP were identified to improve pharmacists' perceptions of EPSs. Results could help to optimize communication and workflow within pharmacies together with reducing cost and appearance of new errors.
Chertow et al. USA [36]	Evaluation of CPOE system by a randomized controlled trial with a crossover design involving 7490 patients.	Decreased MEs and fewer non-intercepted serious MEs; CPOE supported by CDSS decreased EP errors.
Kaushal et al. USA [37]	Systematic review - of 11 randomized controlled studies to determine the effect of CPOE system and CDSS on medication safety.	Significant reduction in specific types of MEs. No significant effect on ADEs in institutions using homegrown systems. The benefits of CPOE with CDSS were reduced numbers of ADEs and MEs with increased cost containment.
Tan et al. Singapore [38]	A survey evaluating users' (n=179) satisfaction with EPS and associated factors in PHC setting.	The participants reported satisfaction with EPS and indicated that EPS reduced MEs. Some concerns were raised about functionality of EPS and focus was more on productivity rather than care.
Gandhi et al. USA [39]	Prospective cohort study of four adult PHC practices in Boston that examined 1879 e-prescriptions.	Prevalence of EP errors was 7.6% and 3% of all prescriptions had potential ADEs. Concluded that more advanced HIT systems need to be integrated.
Yoon et al. Korea [40]	A quantitative study to develop a simple method of evaluating physicians' prescription patterns and their level of awareness of	Found the prescription patterns for hyperkalemia and clostridium difficile-associated diarrhea were well correlated with physicians' knowledge. Accordingly, this algorithm would enable

Study	Study theme, setting and areas	Study results and comments
	clinical practice guidelines.	quantification of prescribers' adherence to clinical guidelines and thereby improve prescribing practices.
Koppel et al. USA [41]	Mixed-method study at urban teaching hospital included 261 house staff, 88% of whom were CPOE users.	CPOE system facilitated 22 types of ME risks. This study needs replication by using advanced and certified EHR with EPS.
Beard & Smith UK [42]	This case study aimed to quantify EP error rate and efficiency of EP linked with a robotic dispensing machines in 1000-bed hospital.	Dispensing errors were not adversely affected and overall efficiency was improved. The direct linking of EP to a robotic dispensing system produces increased efficiency and improves quality of the dispensing process.
Donyai et al. UK [43]	Studied a 28-bed general surgery ward in a teaching hospital and explored the effects of EP on prescribing quality.	A significant reduction in MEs resulted in less pharmacist intervention. The use of EPS improves the quality of e-prescribing.
Lehnbom et al. Australia [44]	This qualitative study using phone interviews that explored opinions of Swedish consumers and health professionals regarding shared EHRs.	Professionals viewed regionally shared EHRs as facilitating a holistic patient approach, assisted in patient follow-up, and reduced overprescribing. Consumers showed a poor knowledge about shared EHRs and the National Patients Summary (NPS) and hence needed training to facilitate EHRs and NPS utility.
Estellat et al. France [45]	A prospective study with a mixed-design in a university hospital. All medication order lines (MOLs) were collected during 5 days using a CPOE system for drug prescription.	A total of 399 (11%) modified-prescription MOLs corresponding to 222 (52%) patients required a pharmacy alert. Among the 81 pharmacy alerts targeted to the prescriber, 21 (26%) resulted in modification of the prescription. Pharmacy validation provided moderate benefits through CPOE system.
Barber et al. UK [46]	A qualitative socio-technical evaluation study of integrated EP and administration system on one surgical ward in a teaching hospital. Participants included staff on ward and pharmacy.	Functionality of EPSs improved over time and associated with staff attitude changes.
Devine et al. USA [47]	A quasi-experimental evaluation study with pre- and post-test design compared prescriptions written before and after implementation of a CPOE in a community based multispecialty group practice.	Frequency of errors declined from 18.2% to 8.2%. The largest reductions were observed in illegibility (97%), use of inappropriate abbreviations (94%), and missing information (85%). There was a 57% reduction in potential ADEs/near misses. CPOE system significantly reduced several types and severity of MEs.
Krania et al. Greece [48]	Aim was to evaluate physicians' attitudes towards EP to identify potential improvements.	Physicians were satisfied with EP. Key barriers, however, were system unavailability, time to adjust and adapt to EP, management issues, lack of training, HIT requirements and medical coding limitations. Strategies to realize the benefits of EPS by physicians were suggested.
Fischer et al. USA [49]	A pre- and post-test design study with concurrent controls evaluated effect of EP with	EP resulted in a 3.3% increase in tier 1 prescribing and prescriptions for tier 2 and 3 prescribing decreased. The use of EPS with FDS

Study	Study theme, setting and areas	Study results and comments
Stone et al. USA [50]	formulary decision support (FDS) using 18 months administrative data of two large Massachusetts insurers.	could result in medication cost reductions.
Ammenwerth et al. Austria [51]	A retrospective and prospective analyses of patient-safety measures, pre- and post-CPOE, academic multispecialty practice	Surgical errors were substantially reduced with enhanced work efficiency; however, technology refinements are needed for patient safety.
Astrand et al. Sweden [52]	A systematic review of 25 eligible studies that evaluated the effect of CPOE/EPs on reduction of MEs, potential ADEs and ADEs in different clinical and geographic settings.	Most of the studies analyzed the effect on the rate of MEs, potential ADEs and ADEs showed a significant reduction in relative risk. Reporting quality and study quality was limited and more RCTs that should include wider geographic and clinical settings are needed to further support the impact of medical informatics on ME reduction.
Hsiao et al. USA [53]	Direct observational study at three Swedish mail-order pharmacies compared new electronic and paper prescriptions.	Of the 31,225 prescriptions dispensed, clarification contact was made for 2.0% of new e-prescriptions and 1.2% of new paper prescriptions. Electronic transfer of prescription (ETP) technology is needed to be move toward better two-way communication between the prescriber and pharmacist with automation checks.
Sketris et al. Canada [54]	This study used the 2008-2009 National Ambulatory Medical Care Survey data to examine the relationship between EMRs and 7 quality measures in physician offices.	EMRs were associated with lower odds of blood pressure check, inappropriate urinalyses, and prescription of antibiotics for URI compared with no EMRs. The patient problem list was associated with higher odds of inappropriate prescribing for elderly patients. The results show both positive and inverse relationships between EMRs features and quality of care.
Baysari et al. Australia [55]	This review article discusses medication-use system, identifies factors affecting prescribing, and assesses effectiveness of interventions.	Factors related to patient, prescriber and drugs determine e-prescribing and use of effective multifaceted interventions. No single approach was appropriate for every prescribing problem, and prescriber practice
Isaac et al. USA [56]	An audit of electronic inpatient charts for assessing alerts initiated by EPS when its functions were used or not used by prescribers in a teaching hospital.	Alerts related to therapeutic duplications were most frequent and one fifth of them were preventable contingent on proper use of EPS functions by prescribers. Updated EPS should produce meaningful alerts, which need to be addressed by trained prescribers for reducing MEs.
Weingart et al. USA [57]	Retrospective analysis of 233,537 medication safety alerts generated by 2872 clinicians using a common EPS in ambulatory care. Multivariate techniques were used to examine factors associated with alert acceptance.	A total of 6.6% e-prescriptions generated alerts. Clinicians accepted alerts - 9.2% of DDI, 23.0% of allergy, and high-severity interactions (61.6%). No difference in alert acceptance was found among clinicians of different specialties, who tended to override most medication alerts. The current medication safety alerts are inadequate for patient safety.
	A survey of 300 Massachusetts ambulatory care clinicians (61% response rate) assessed participants' satisfaction with	Participants responded; EP improved the quality of care (78%), prevented MEs (83%), and enhanced patient satisfaction (71%) and clinician efficiency (75%); alerts helped 35% of

Study	Study theme, setting and areas	Study results and comments
	EPSs, their perceptions both of alerts and behavior changes from alerts.	prescribers to modify a potentially dangerous prescription. Less than 50% were satisfied with drug interaction and allergy alerts. Excessively generated alerts remain a problem.
Franklin et al. UK [58]	This study sought to document numbers and types of interventions by community pharmacists and related staff using EPS release type (EPSR2), compared with other types, and comment on potential effects of EPSR2 on pharmacy practice.	Eight pharmacies five with EPSR2 reported 69 problems with 68 prescriptions; 33 clinical, 6 logistical or organizational, and 30 unsigned prescriptions related to non-EPSR2 and eight were primarily related to EPSR2 functionality. Prescribers should consider the compatibility of regularly prescribed items with the NHS dictionary of medicines and devices.
Reckmann et al. USA [59]	Systematic review of CPOE systems among hospital inpatients;13 papers reporting 12 studies were identified	Nine demonstrated a significant reduction in prescribing error rate for all or some drug types. Few studies examined changes in error severity. Minor errors were decreased. However, the effectiveness of CPOE systems in reducing PEs in inpatients was not compelling and was limited by modest study sample sizes and designs.
Bell et al. USA [60]	This research described the development, implementation, and evaluation of active CDSS for multiple pharmacogenetic test results that were reported preemptively.	Pharmacogenetic rules implemented for risk drugs and issued alerts resulted in the interruptive CDSS that appropriately guided prescribing in 95% of patients. It is feasible to develop computational systems that provide clinicians with actionable alerts for gene-based drug prescribing at the point of care.
Hellström et al. Sweden [61]	A web-based survey of physicians from PHC and hospital clinics aimed to evaluate their attitudes toward EP	EHR systems were considered generally easy to use with provision of better services. EP was considered as time saving and safe. Physicians were satisfied with EHRs and identified weaknesses that call for updated EHR.
Baysari et al. Australia[62]	Using Delphi technique, a qualitative study aimed to reach consensus among prescribers on the usefulness of alerts and strategies for reducing insignificant alerts within EPS.	Prescribers agreed allergy and intolerance alerts should be retained. Involving prescribers in customization of alerts is a successful approach.
Devine et al. USA [63]	Cross-sectional study to elicit physician and staff perceptions of EPS implementation using focus group approach	Among the ten themes, especially positive attitudes facilitated the adoption of CPOE. Both prescribers and staff worked through the transition to successfully adopt EP with several benefits.
Kirkendall et al. USA [64]	This study assessed the accuracy of vendor-supplied dosing electronic rules (ERs)(n=750) for pediatric medical orders . Seven months of MOs for 30 medications and alerts were analyzed across 5 age ranges and 5 dosing	Accuracy of ERs was 55.1% and 57.6% with a priori age range and over the lifetime, respectively. ERs relating to the newborn age were similarly accurate. The accuracy of ERs is suboptimal and further research is warranted for understanding the effects of ERs on safe EP in pediatric population.
Duffy et al. USA [65]	A study of telephone logs that obtained data from the hand-written after-hours telephone logs and surveys of patients and	After-hours calls were reduced by 22% but the number of medication calls significantly increased. Both provider and patients were satisfied with the EPS, despite a paradoxical

Study	Study theme, setting and areas	Study results and comments
	providers. The after-hours calls were reviewed before, immediately after and 1 year after the initiation of an EPS.	increase in medication-related calls
Sweidan et al. Australia [66]	Modified Delphi technique employed to reach consensus on the impact of EPS features in four domains	From 114 software features, 68% had a high positive impact in at least one domain, 32% had a medium impact, and 24% features had a high positive impact across three or four domains. The features of EPSs support safety and quality in EP of medicines in PHC.
Kazemi et al. Iran [67]	A prospective study explored nursing order entry (NOE) versus CPOE in a neonatal teaching hospital	MEs including overdose decreased significantly during NOE compared with POE. NOE increases physicians' compliance and reduce non-intercepted MEs more effectively than POE. NOE might be an option in case of physicians resist EP
Jani et al. UK [68]	CDSS alerts study at a pediatric hospital. Retrospective review of CDSS alerts recorded in the EPS over a period of 1 year	16,182 conflict alerts were recorded when ordering 26,836 items, and 3507 were visible to the user. Users overrode 89% of visible alerts. Drug-allergy and drug duplication alerts were the most and least accepted, respectively. A high incidence of alert override is undesirable and hence EPSs need to be redesigned
Taegtmeyer et al. Switzerland [69]	Eight clinical pharmacologists reviewed electronic or paper records of 502 patients hospitalized in a large teaching hospital	158 medication problems identified in 109 hospital admissions received 145 recommendations, of which 51% were implemented. Admissions with an electronic chart had 2.74-times higher odds for comply with the change compared to a paper chart. EP was associated with improved drug safety
Spina et al. USA [70]	A cross-sectional study, using a 35-item questionnaire, explored Veterans Affairs (VA) physician based practices nationwide	72% reported documenting outside medications, but only 44% entered them in the non-VA medication data. 88% reported serious allergic or ADRs, which were notified to a pharmacist. CPOE checks improved EP safety.
Nanji et al. USA [71]	Retrospective cohort study of 3850 e-prescriptions received by an outpatient pharmacies across three states over 4 weeks	11.7% e-prescriptions contained errors, of which 35% were potential ADEs. Error rates varied by EPS, from 5% to 38%, and the omission type (61%) was the modal error. Some EPSs prevent errors better than others
Redwood et al. UK [72]	An exploratory survey of routinely collected medication incidents over 5 months	Of 485 incidents, 15% were distinguished as socio-technical. Implementers of EP system need to rectify unintended MEs and should emphasize on training of prescribers.
Bramble et al. USA [73]	Using two focus groups, a qualitative study of providers and nurses aims to identify safety measures in a rural community ambulatory care practice with an EHR.	Three themes including EHR with EP adoption led to new improvements for patient safety, affected efficiency in clinics, and workarounds. Safety concerns differed between groups. EHR improvements should match the differing needs of professionals who deliver healthcare.
Classen et al. USA [74]	A review of leading critical DDI approaches for use in EHR systems with CPOE	Implementation of DDI checking is key to realizing the benefits of EP with respect to patient safety, which is further enhanced by the ONC and Leapfrog DDI lists.

Study	Study theme, setting and areas	Study results and comments
Robertson et al. Australia [75]	A study in general practice setting focused on clinical information and CDSSs	CDSS development must recognize the time pressures of general practice, preference for integration, and cost concerns. Without standards, the benefits of computerization on patient safety and outcomes will be minimal.
Jariwala et al. USA [76]	Internet-based survey of primary care physicians (PCPs) – EP users versus nonusers	Electronic prescribers (83%) reported satisfaction with their EPS and a preference for EP over traditional prescribing. About 50% of the PCPs experienced problems with EP. PCPs tend to have problems in using EPS.
Schnall et al. USA [77]	This pre- and post-design study explores the use of e-alerts in the screening of HIV disease in emergency setting.	The use of the electronic alert significantly increased offering an HIV test and resulted in a high number of HIV testing. The use of electronic hard stop alerts improves HIV screening.
Coleman et al. UK [78]	Use of historical data on EP to derive dose-range limits	Dosing decision support within EPS can be derived by statistical analysis of historical prescription data. Through dose-checking rules, prescribers could be alerted to potentially toxic doses.
Westbrook et al. Australia [79]	A pre-post design study to evaluate the effectiveness of two commercial EPSs among inpatients	The EP reduces the rate of MEs attributable to a large reduction in unclear, illegible, and incomplete orders. Each EPS revealed different types of system-related errors, which call for redesigning of system and users training.
Lau et al, Canada [80]	Systematic review of 27 controlled and 16 descriptive studies on the impact of EMRs that examined six areas including patient-physician interaction	Half of the studies and half of the individual measures had positive impact while 18.6% of the studies and 18.3% of the measures had negative impact. Currently, there is limited positive impact of EMRs in the physician's office.
Galligan et al. USA [81]	A community-based study examined the rate of pharmacist interventions in electronic and traditional prescriptions in pharmacies	No significant differences between electronic and traditional prescriptions with regard to pharmacist intervention were found. This study needs replication.
van Doormaal JE et al. Holland [82]	An interrupted time-series study evaluated the impact of CPOE/CDSS on incidence of MEs and preventable adverse drug reactions (ADRs)	Though MEs were reduced considerably, no effect on ADEs was discerned
Jariwala et al. USA [83]	Internet-based survey of PHC physicians, e-prescribers versus non-e-prescribers and responders were 443.	EP was encouraged by software features. Pre-implementation and cost factors were most discouraging issues. EP adopters should target discouraging factors for facilitating EP in health settings.
Lander et al. USA [84]	A cross-sectional survey of nonparticipating pharmacies' pharmacists perceptions about barriers against EP	43% reported plans to implement EP and 39% reported no such intention. Both cited similar reasons. Main barriers to EP were costs and transaction fees across both adopters and non-adopters of EP
Went et al. USA [85]	A comparison of EP with paper prescription included charts of 16 intensive care unit (ICU) patients in PHC	Increased compliance with national standards and significantly reduced MEs in e-prescriptions (8.5%) than handwritten prescriptions (51%). A well designed EPS increases patient safety

Study	Study theme, setting and areas	Study results and comments
Weingardt et al. USA [86]	A qualitative study used 3 focus groups of 25 high volume physicians from different specialties in Massachusetts for exploring the use and value of EP and medication safety alerts in small and medium-size practices.	Financial incentives by insurers encouraged use of EP. Overriding of medication safety alerts by physicians remains a problem, though some drug allergy and DDI alerts are of important concerns for patient safety.

According to some investigators, electronic prescribing is a social art and hence the design and implementation of EPs should address the sociocultural context of EP. Furthermore, especially in primary care where health problems are often ill defined, studies need to take into account the sociotechnical character of EPs [91]. It is widely believed that HIT saves time and increases efficiency is often based on assumptions of the fungibility of time and people. Units of time added or saved on different steps of the work flow can be summed up, and thus reveal any net efficiency gain. But workflow time savings involve changes in the quality of tasks and redistribution of work and responsibility, so that time can hardly be added or subtracted to obtain 'efficiency totals' [92]. In an exploratory survey of healthcare providers in 11 general practices, Makam et al. reported variable responses of participants about utilization of key functions of EHRs with some degree of dissatisfaction. Both dissatisfaction with and suboptimal use of the EHR may minimize the potential for EHR use to improve healthcare in terms of preventive and chronic disease management. Makam et al. suggested [93] that future work should optimize use of key functions and improve providers' time efficiency. One study involving community-based practices reported that predictors of e-prescribing were younger physicians, pediatricians, and prescribers affiliated to larger practices [94]. The reasons underlying prescribers' variable e-prescribing need to be explored in future, the study suggested. Nonetheless in USA, more than 50% of health providers and majority of pharmacies are e-prescribing via EHR and accepting e-prescriptions, respectively [95]. A Canadian study in PHC reported that the adoption of EP, a highly challenging task, contingent on novel physician-related factors in terms of information-acquisition style and practice-related variables, such as prevalence of medication use, influence the adoption of EP [96]. Notably, underserved communities including minorities, low income group and metropolitan status tend to have low

adoption of EHR. Therefore, there is substantial room for increased EHR adoption across the United States especially in underserved areas. Authors suggested further research to monitor policy initiatives in these areas and examine sources of heterogeneity in low- and high-adoption communities [97].

3.5 Studies on CPOE and CDS System

The implementation of CPOE and CDSSs to safeguard drug treatment is disseminating globally [98]. A landmark study performed at a major teaching hospital that utilizes a widely used leading CPOE telephone and data system, found that the CPOE system facilitated the occurrence of 22 types of MEs [41]. Two more studies evaluated the CPOE system and collectively found a decrease both in MEs and non-intercepted serious MEs [36,43]. The effects of EP on prescribing quality, as indicated by prescribing errors and pharmacists' clinical interventions, have also been investigated [43]. The MEs and interventions were recorded by the ward pharmacist during a 4-week period. According to this study, EPS improved the quality of EP by reducing both prescribing errors and pharmacists' clinical interventions [43]. A comparison of 55,016 handwritten prescriptions versus 55,153 e-prescriptions was undertaken at a physician-owned multi-specialty clinic system [47]. The results of this research suggested that a basic CPOE system in a community setting was associated with a significant reduction in MEs of most types and severity levels. Notably, chemotherapy prescribing errors occurred even with EP. Aita and colleagues suggested periodic audits and set-up correction before implementation of the CPOE system [99].

Kaushal and associates performed a systematic review to determine the effect of CPOE and CDSSs on medication safety [37]. Based on several observations, they found it would be beneficial to study the differences between different commercial systems that have not been

properly evaluated or compared with systems in the literature [37]. According to other researchers [75], CDSS developers must recognize the time pressures experienced in PHC practice, the preference for high-quality information resource integration, the cost concerns and minimum standards, and the anticipated benefits of computerization on patient safety and health outcomes. In another study, researchers compared the change in prescriptions for three formulary tiers before and after EP were implemented, estimated potential savings, and developed multivariate longitudinal models to estimate the effect of EP when controlling for baseline differences between intervention and control prescribers [49]. The investigators concluded that clinicians using EP with formulary decision support were more likely to prescribe tier 1 medications, which are associated with substantial financial savings.

In a systematic review of CPOE systems, researchers observed mixed results, including reduction in MEs but increases in the rate of duplicate orders and failures to discontinue drugs, often attributed to inappropriate selection from a dropdown list or to an inability to view all active medication orders concurrently [59]. The investigators recommended that future studies include larger samples and multiple sites, have controlled study designs and standardized error and severity reporting, and discuss the role of CDSSs in minimizing severe prescribing errors. In qualitative research employing the focus group method involving 70 participants and eight focus groups and a semi-structured questionnaire, Devine and colleagues [63] explored prescriber (n = 17) and staff (n = 53) perceptions of a CPOE system and identified ten themes – including prescribing efficiencies, safer care, time efficiencies, enhanced communication with patients and pharmacists, and positive attitudes – that facilitated adoption. Their findings support the results of other researchers on EHR and EP [61]. Other researchers have reported that transitioning from older EHR systems to newer commercial EHR systems with CDSSs and EP is extremely difficult, too complex, and reduces physician efficiency [11]. In yet another study, both provider and patient satisfaction with EP was very high, with a reduction in total after-hours calls, despite a paradoxical increase in medication-related calls [65]. The researchers suggested further study is warranted to document other evidence-based outcomes of EP.

A minority of physicians were found to resist EP and be frustrated by using CPOE in a study that also found that the rate of non-intercepted MEs during a period when nurse order entry (NOE) was used was 40% lower than during a period when physician order entry was used ($P < 0.001$) [67]. The same study also reported other significant results, including that the severity of overdose errors was lower in the NOE period ($P < 0.02$). Accordingly, NOE can increase physicians' compliance with warnings, recommended doses, and frequency, and reduce non-intercepted medication dosing errors as effectively as, or even more than, physician order entry. Further, in case of physicians' resistance to CPOE implementation, NOE may be considered a beneficial alternative order-entry method [67]. In another review, Clyne and associates provided evidence that health care providers were satisfied with EPSs and CDSSs [100]. They viewed the EPSs as having a positive impact on the safety of their prescribing practices. However, the problem of overriding or ignoring alerts persisted. The investigators suggested further investigation as to find out the solution for overriding alerts. In another systematic review of relevant literature, the research team evaluated the effect of CDSSs on clinical outcomes, health care processes, workload and efficiency, patient satisfaction, cost, and provider use and implementation [101]. A total of 148 randomized controlled trials were included in that review. Of these, 128 (86%) assessed health care process measures, 29 (20%) assessed clinical outcomes, and 22 (15%) measured costs. They found that both commercially and locally developed CDSSs improved health care process measures related to performing preventive services, ordering clinical studies, and prescribing therapies. Investigators concluded both commercially and locally developed CDSSs are effective at improving healthcare process measures across diverse settings, but evidence for clinical, economic, workload and efficiency outcomes remains sparse [101].

3.6 Studies on Generated Alerts by EP System

Researchers in a retrospective study addressed clinicians' overriding of alerts generated through EPSs and found that clinicians accepted significantly more high-severity alerts than moderate- or low-severity interaction alerts (10.4%, 7.3%, and 7.1%, respectively; $P < 0.001$) [56]. Furthermore, clinicians accepted 2.2% to

43.1% of high-severity interaction alerts related to classes of interacting medications and were less likely to accept a drug-drug interaction (DDI) alert if the patient had previously received the alerted medication. It was concluded that clinicians override most medication alerts, suggesting that current medication safety alerts may be inadequate to protect patient safety. In a systematic review and meta-analysis of 36 eligible studies of computerized drug-lab alerts to improve medication-related outcomes, Bayoumi et al. reported that drug-lab alerts did not reduce rate of ADEs, length of hospital stay, likelihood of bleeding time and hypoglycemia but were associated with likelihood of prescribing changes/processes and lab monitoring [102]. In a study of medication-related CDSS generated alerts, Nanji and associates reported alert rate of 7.9% and an override alert rate of 52.6%. They reported that the most common alerts were related to duplicate drugs, patient allergy, and DDI. Most commonly overridden alerts were formulary substitutions, age-based recommendations, and renal recommendations. Furthermore, an average of 53% of overrides were classified as appropriate but varied by alert type from 12% for renal recommendations to 92% for patient allergies. These alerts need refinement in order to improve the relevance of alerts and reduce alert fatigue [103]. Furthermore, one study has addressed the issues of specificity of DDI alerts, types of alerts in the form of dynamic and static, alert burden, and suggested causes of and counterstrategies especially refinement of knowledge bases for overriding alerts [104].

In a survey of the perceptions of commercial EPS users with a 61% response rate, investigators made multiple observations [57]. Perceived advantages included being able to: counsel patients about potential reactions (49%), look up information in medical references (44%), change the way a patient was monitored (33%), and take action other than discontinuing or modifying an alerted prescription (63%). Further, 47% were satisfied with the DDIs and allergy alerts. Perceived problems included alerts triggered by discontinued medications (58%), alerts that failed to account for appropriate drug combinations (46%), and an excessive volume of alerts (37%). Although clinicians were critical of the quality of EP alerts, these alerts may lead to clinically significant modifications in patient management that are not readily apparent based on acceptance rates [57]. In a UK study, Jani and colleagues retrospectively explored the

characteristics of CDSS alerts generated over a year and found a high number of undesirable alerts were overridden, which is consistent other reports in the literature [68]. This suggests that the underlying algorithms for alert generation in the studied EPSs are unspecific and need to be reviewed [68]. In a scenario-based study of junior doctors, a team of UK researchers addressed how to make EP alerts more effective. They found that modal alerts were over three times more effective than non-modal alerts and provided new evidence about the relative effects of modal and non-modal alerts on EP outcomes [105]. Spina et al. conducted a national survey of VA physicians and observed some important responses, including that 90% of providers felt that the VA EPS improved prescribing safety to some degree and 48% of providers described critical DDI alerts as very useful [70]. Overall, all participants thought that CPOE improved prescribing safety with variable entry of relevant information into the appropriate electronic fields.

3.7 Studies on EPS-facilitated MEs

EPSs can introduce new MEs [41,105-106]. This was also suggested by a study conducted in a large acute hospital in the UK, which implemented a prescribing, information and communication system [72]. Incidents were grouped into socio-technical and non-socio-technical, and the former type tended to occur at the point at which the system and the professional intersected. It was determined that these would not have occurred in the absence of the system. Of all incidents, 15% were observed to be socio-technical. The researchers concluded that an EPS has the potential to give rise to new types of risks to patient safety; hence, the clinical and technical implementers of EPSs must design out unintended problems, highlight training requirements, and revise clinical practice protocols [72]. A recent systematic review of more than 176 eligible RCT and NCRT reported that only a minority of studies that investigated these EPS and EHR interventions included threats to patients' safety as outcomes or monitored for adverse events in ambulatory care. Therefore, more research is needed to focus on the draw-backs and negative outcomes that implementation of these interventions might introduce [107]. Pharmacists' interventions tend to decrease user and EPS related prescribing errors at patient discharge in academic hospitals in the UK and these errors by definition are mostly near misses or close calls [108]. In a recent controlled study of two hospitals,

Westbrook and colleagues found that both hospitals experienced system-related errors (0.73 per admission in one hospital and 0.51 in the other) [79]. In turn, this accounted for 35% of post-system errors in the intervention wards. However, implementation of commercial EPSs resulted in statistically significant reductions in prescribing error rates. Although the reductions in clinical errors were limited by the absence of CDSSs, a statistically significant decline in serious errors was observed. They suggested that while system-related errors require close attention as they are frequent, they are potentially remediable by system redesign and user training [8,79]. Some limitations of their study were a lack of control wards in hospital B and an inability to randomize wards to the intervention [79].

3.8 EP Studies in Pediatric and Geriatric Setting

The literature suggests that dosing errors, overprescribing of anti-infective agents and administration route are major problems in pediatric and elderly clinical practice that require pharmacists' interventions [108-111]. Coleman and associates studied dose-range limits in EPSs that could be derived by statistical analysis of historical prescription data. As a corollary, this research team suggested a combined theoretical and statistical derivation of dose-checking rules to ensure that prescribers are alerted appropriately to potentially toxic doses [36]. To address the same issue, researchers developed an evaluation model that might be used not only to determine usability in electronic prescribing but also as a basis for studying the usability of other CPOE systems. According to their study, the most urgent improvement necessary to reduce the risk of drugs being prescribed at the incorrect dosage, is the development of a more consistent and intuitive interface for EHRs and an improvement in the dosage function of these EP systems [37] with integration of CDSS especially in pediatric settings [109,111]. Furthermore, pediatric dose rounding is a complex process. To address this issue, investigators conducted a pilot study that used automated dose-rounding algorithm STEPSTOOL. The results suggest that automated dose rounding is feasible mechanism for providing guidance to EPSs and validation of CDSS in order to support targeted and iterative improvement in performance [112]. In a comprehensive report, Johnson and collaborators highlighted that beside some

limitations, the data support the role of EP in mitigating MEs, improving communication with dispensing pharmacists, and improving medication adherence. Consequently the report recommends the adoption of EPSs with pediatric functionality and also supports the policy statement from the American Academy of Pediatrics recommending the adoption of EP by pediatricians [113] and the council recommended a set of functions that technology vendors should provide when EPSs are used in pediatric setting [114].

In geriatric setting, a French descriptive study of 6-month timeline reported that the most frequent drug-related problems (DRPs, total DRPs=241) identified by pharmacists reviewing 311 patients were untreated indication (24.1 %), dose too high (19.1 %), improper administration (12.9 %) and drug interactions (9.5 %). The rate of physicians' acceptance of pharmacists' intervention was 90.0 % with 7.5 % refusals and 2.5 % not assessable. DRPs related to CPOE system misuse (14.5 %), a worrying phenomenon involved errors in selecting dosage or unit and or duplication of therapy. Researchers suggested that the description of the DRPs is an essential step for implementation of targeted clinical pharmacy services in order to optimize pharmacists' job time [115]. An observational study of Belgian nursing homes reported high utilization of potentially inappropriate medication prescribing and recommended computerized drug monitoring system to improve the quality of prescribing in nursing homes [116].

3.9 Studies on Barriers against EP Systems

One progressive report from USA identified major barriers including the inability to electronically transmit prescriptions for controlled substances and confusion about standards for data exchange. Friedman and colleagues suggested further investments to reap the benefits of e-prescribing on a national scale [117]. One of the major barriers preventing widespread adoption is the potential detrimental impact on workflow. However, at least one study using time-motion technique reported that e-prescribing used carefully does not disrupt workflow [118]. Other investigators identified barriers related to maintaining complete patient medication lists, using CDSS, obtaining formulary data and electronically transmitting prescriptions to pharmacies [119]. Furthermore, a study using exhaustive Chi-squared Automatic

Interaction Detection (CHAID) for data segmentation found that one of the barriers for adoption of e-prescription is low physician utilization especially female physicians and Hispanic physicians in a variety of specialties and styles of practices in various health settings. The study concluded that segmentation data analyses help to identify EP adoption barriers and to develop targeted interventions for adopting EPSs in physician practices [120]. Other studies explored pharmacists' and physicians' attitude and views on integrated EPSs and found system unavailability due to technical problems as a barrier for e-prescribing. They also identified the importance of users education and expectation management, though they expressed its usefulness in terms of workflow efficiency and medication management safety [121-123].

In another qualitative study, researchers reported that the electronic transmission of new prescriptions has matured and noted that changes in technical standards and system design and more targeted physician and pharmacy training may be needed to address barriers to electronic renewal, mail-order pharmacy connectivity, and pharmacy processing of e-prescriptions [124]. A cross-sectional study using an internet-based survey administered to a national convenience sample of PHC physicians aimed to determine factors that physicians find encouraging and discouraging about e-prescribing and to compare these factors based on physicians' adoption status. Analyzing 443 surveys, seven e-prescribing factors were identified. Pre-implementation and cost factors were found to be most discouraging. Software features were found to be most encouraging. Current e-prescribers found e-prescribing factors to be more encouraging than future or non-e-prescribers suggests that fear of the unknown may play a role in prescribers' perceptions of e-prescribing and associated software. E-prescribing stakeholders including policymakers should facilitate the adoption of e-prescribing by directly targeting the factors that are most salient to physicians [83].

This study aimed to identify the barriers to adoption of e-prescribing among nonparticipating pharmacies and to describe how the lack of pharmacy participation impacts the ability of physicians to meet meaningful use criteria. Pharmacists/managers from nonparticipating pharmacies were interviewed to determine

barriers to the adoption of e-prescribing. Of the 23 participants, 43% reported plans to implement e-prescribing sometime in the future but delayed participation due to transaction fees and maintenance costs, as well as lack of demand from customers and prescribers to implement e-prescribing. 39% reported no intention to e-prescribe in the future, citing more or less similar reasons reported by implementers. The barriers to e-prescribing identified by both late adopters and those not willing to accept e-prescriptions were similar and mainly involved initial costs and transaction fees associated with each new prescription. One of the strategies for increasing participation was to waive or reimburse transaction fees, based on demographic or financial characteristics of the pharmacy [84].

3.10 Studies on Strategies for Reducing MEs

In a study with pre- and post-intervention design reported that interventions including a closed-loop electronic prescribing, automated dispensing and barcode patient identification system reduce e-prescribing errors and medication administration errors, and increased confirmation of patient identity before medication administration. Furthermore, it was observed that time spent on medication-related tasks increased [125]. In another pre-post study, Westbrook and colleagues explored the impact of electronic medication management system (eMMS) on doctors and nurses work timeline related to patient safety and medication management. The study found that eMMS introduction did not take time away from direct care or affect medication tasks. Work patterns observed on these intervention wards were associated with previously reported significant reductions in prescribing error rates compared to the control wards [126]. In a survey of Spanish hospitals, investigators suggested that the implementation of automated medication dispensing cabinets need integration with e-prescribing, identified safety practices and other technical, organizational and system monitoring safety issues for minimizing medication errors [127]. However, in a recent quasi-experimental study, El-Said et al. reported that implementing standardized chemotherapy-prescribing templates significantly reduced all types of prescribing errors and improved chemotherapy safety [128]. One USA study that explored medication error discrepancy rate across three ambulatory care settings suggested that to reduce MEs, a better understanding is needed of

the sources of discrepancies that occur within the prescriber's clinic, and those that occur between the clinic and pharmacy [129].

However, according to one study, EP data generated by junior doctors in a large teaching hospitals setting could not identify doctors who were at higher risk of making serious medication prescribing errors and called for the evaluation of data from a quality assurance perspective for this purpose [130]. By extension, doctors who make more MEs need to be identified and trained in EPS. This could be one of the strategies for preventing serious MEs. Furthermore, using secondary EP and CDSS data from an acute hospital, Dixon-Woods and colleagues reported that unintended consequences in terms of the risk of focusing attention on aspects of patient safety made visible by EHR system at the expense of other, less measurable but nonetheless important, concerns need to be avoided for improving quality and safety of patient care [131].

In another study, Lapane and colleagues found that clinicians and their staff confirmed that efficiencies were realized with the adoption of EP [132]. These related to knowledge of formularies, processing refills, and decreasing errors. The researchers suggested that opportunities to improve efficiencies could be realized by assuring correct information in the system. A toolkit is developed to support implementation of EPS into UK hospitals [133].

In a study of 3850 e-prescriptions, a clinician panel reviewed the e-prescriptions to identify and classify MEs with clear primary outcomes in terms of the incidence of MEs, potential adverse drug events (ADEs), and rate of prescribing errors by error type and prescribing system [71]. Based on their observations, the researchers suggested that any EPS due to be implemented needs to have comprehensive functionality and processes in place to ensure meaningful system use to decrease MEs and enhance patient safety. In a study of prescribing errors in a hospital setting, 15% of paper prescriptions and 8% of e-prescriptions were observed to have errors [134]. This indicates that EP decreases paper prescription errors by about 50%.

Classen and colleagues reviewed the leading critical DDI lists from multiple sources including the new USA Office of the National Coordinator for Health Information list [74]. According to their review, the Office of the National Coordinator list

will make it easier for health organizations to ensure they are including the most important DDIs and the Leapfrog List may help these organizations develop an operational DDI list that can be practically implemented. Further, they identified seven common DDIs that could be the starting point for all health organizations in terms of medication safety. Malone and colleagues addressed the issue of prevention of DDIs using a stand-alone medication management program installed in a wireless palm top computer device [135]. They observed that most prescribers did not use the device to update patient medication histories and that the device was not associated with a reduction in the rate of clinically important DDIs.

3.11 EP-Pharmacist Intervention Studies

Another study sought to describe pharmacists' interventions during the validation of e-prescriptions, the impact of these interventions on the prescribing process, and the extent to which CPOE was responsible for the errors identified by the pharmacists. All medication orders were reviewed by the pharmacists, who described the frequency of pharmacist alerts and the short-term impact of these on the correction of potential prescribing errors. According to this study, pharmacy validation, which was associated with only a moderate short-term impact on the reduction of MEs, may also provide benefits by identifying necessary improvements in the CPOE system [45]. Pharmacists' interventions tend to be more effective when CPOE is connected to a ward pharmacist as found in a French study of seven teaching hospitals. Pharmacists intercept a variety of drug-related problems which mainly include non-conformity to guidelines or contraindications, too high doses, DDI and improper administration. The interventions consisted of changes in drug choice (41%), dose adjustment (23%), drug monitoring (19%) and optimization of administration (17%). Interventions were communicated via the CPOE in 57% of cases and 43% orally. The rate of physicians' acceptance was 79.2%. In multivariate analysis, acceptance was significantly associated with the physician's status, method of communication, and type of recommendation [136].

In an observational study, Swedish investigators assessed 31,225 prescriptions and found that 89.5% of the suggested pharmacist interventions were accepted by the prescriber, and further

reported increased clarification contacts for new e-prescriptions compared with new non-e-prescriptions/paper prescriptions [52]. It was suggested that electronic transfer of prescription technology should be developed for two-way communication between the prescriber and the pharmacist, with automated checks of missing, inaccurate, or ambiguous information to enhance safety, quality, efficiency, and cost-effectiveness within the health care system [52]. In a review article, multiple factors were found to affect EP and interventions reported as effective were multifaceted [54]. The reviewers concluded that no single approach is appropriate for every prescribing problem, prescriber practice, or health care setting. Interventions with variable effect sizes have multiple mechanisms that affect their effectiveness. Further research is needed to determine how or why various interventions work and to identify barriers to effective implementation [54].

Taegtmeier et al. [69] conducted a study of the electronic and paper charts of 502 patients to assess the drug-related problems and time delays with proposed recommendations. Besides other observations, the researchers found that the time delay between recommendations being made and their implementation was minimal – a median of 1 day – and did not differ significantly between the two different chart systems. EP in this hospital setting was associated with increased implementation of clinical pharmacologists' recommendations for improving drug safety when compared with paper-based prescribing. In a recent study of paper and e-prescriptions requiring pharmacists' interventions, Gilligan et al. found that pharmacists' interventions did not differ significantly. The authors suggested that pharmacists must intervene on e-prescriptions at the same rate as they do with handwritten prescriptions [81]. From pharmaceutical care perspective, standardizing definitions and terminology of medication adherence and persistence in research is crucial when using electronic databases [137].

3.12 Applications of EPS and EHR

Most of studies on e-prescribing, EHRs, EMR and COPE have focused on medication errors and very few have evaluated other uses and clinical end outcome. One retrospective cohort study reported that EP with formulary decision support improve low density lipoproteins goal achievement attributed to improved adherence to

more affordable treatment [138]. In a retrospective study of e-prescriptions in academic setting with interrupted time-series design to assess the rate of generic prescribing pre- and post-implementation of generic substitution decision support, Stenner and associates reported that generic substitution decision support system results in rapid improvement in generic e-prescribing across all specialties in academic institutions [139]. In a study of electronic prescription data utilized to assess antibiotics use policy compliance, Baysari et al. found that feedback intervention to prescribers has no impact on policy compliance and identified many problems including policy approval process during data auditing. They recommended that interviews with prescribers should be addressed before applying policy of antibiotic stewardship into EPS [140]. In another study, better results were reported and heart failure core metrics compatible with decline in Angiotensin Converting Enzyme Inhibitors/Angiotensin Receptors Blockers (ACEI/ARB) prescribing both improved during computer based CDSS [141]. Furthermore, electronic prescribing system integrated with CDSS also helped to reduce overuse of antibiotic prescriptions in uncomplicated acute bronchitis in primary care settings [142-144].

Patients with renal insufficiency need drug dose adjustments for avoiding complications. This was addressed in a university hospital based study that used EPS integrated with CDSS and automated reporting of glomerular filtration rate. They found that such patients may still be at risk of developing adverse events and complications [145]. Furthermore, integrated EPS have many uses in different health settings including radiology, critical care, emergency services, [146-148]. An EPS integrated with CPOE helps in prevention of HBV reactivation in patients treated with biological therapy [149].

Furthermore, other useful applications of HIT and e-health include patient adherence to inhaler asthma therapy [150], validation of chemotherapy regimen with increased pharmacists efficiency and improved providers satisfaction [151], unequivocal compliance with antibiotic use and prescribing policy [140], development of evidence-based oncology practice, standardize supportive care, and enhance patient safety [152], low-density lipoprotein cholesterol (LDL-C) goal attainment [153] and parenteral nutrition prescription software development and its integration with

EMRs that help in improving clinical services [154] and delivery of evidence-based intervention in a predictable way in critical care setting [155].

Notably EHRs help in other multiple ways; to prove or refute polypharmacy that has equivocal support of prescribers [156]; to assess the pattern of type 2 diabetes mellitus (T2DM) medication prescription [157] and to use large databases for research [158]. Furthermore, hospital EPS helps in assessing the net ingredient costs of most commonly prescribed medications by new doctors in UK, as was found in a retrospective study conducted in a teaching hospital. However, there remains considerable variation in the total costs of medications uneconomically prescribed by newly qualified doctors [159]. A recent systematic review focused on the impacts of several EMRs areas on physicians' offices [80]. This review examined six areas: (1) prescribing support, (2) disease management, (3) clinical documentation, (4) work practice, (5) preventive care, and (6) patient-physician interaction. A total of 48 distinct factors were identified that influenced EMR success. The review identified several lessons learned regarding necessary factors that were repeated across studies. These were: having robust EMR features that support clinical use, redesigning EMR-supported work practices for optimal fit, demonstrating value for money, having realistic expectations on implementation, and, most importantly, engaging patients in the process. The reviewers concluded that currently there is limited positive EMR impact in physicians' offices [80].

3.13 Local e-prescribing Landscape

Few studies have explored EP in the KSA and only indirectly. One study has reviewed the implementation of EHRs [160]. Another study has qualitatively explored clinicians' perceptions of CPOE system in the ICU of a leading health care organization [161]. In the latter study, researchers surveyed 43 clinicians to assess perceptions regarding 32 factors collected from the literature related to the successful implementation of the CPOE system [161]. The factors identified most critical for success were the provision of training prior to system implementation, adequate clinical resources during implementation, and allowing sufficient time for ordering medication. Researchers concluded that the benefits expected were much higher than the risks and that CPOE reduced MEs and improved quality of care and patient

safety. Two recent surveys about the hospital pharmacy practices in Saudi Arabia found that about one-third (34.5%) of hospitals have CPOE systems with CDSSs and over half (51.9%) have EMR/EHR system in place [162]. For medication dispensing, 21% of hospitals routinely use bar coding technology with automated dispensing cabinets, and for medication administration, 33% use electronic medication administration records (eMARs), 7.4% have bar-code-assisted medication administration (BCMA), and 12% have smart infusion pumps [163]. According to this research, hospital pharmacy practices including prescribing, transcribing, dispensing, and administration are all well developed. Among recommendations made was the use of health informatics including robotic drug dispensing [42]. Both e-prescribing and robotic dispensing of drugs has been shown to substantially reduce medication errors [42,131].

Recently, two studies were conducted on e-prescribing "near misses" in King Saud Medical City [KSMC], Riyadh (164-165). One cross-sectional study evaluated consecutively collected near miss [NMs] report forms [n=1,025] over a period of 6 months in year 2012. Most frequently reported near misses were related to the prescribed medications such as wrong frequency, improper doses, wrong drug, wrong duration, wrong concentration and wrong dosage form. More than half of near misses [55.32%] were identified at transcription and entering stage. About 89% of near misses were made by physicians and nurses whereas pharmacists identified most of the near misses (97.3%) and corrected them by using several strategies including correcting drug-related items and calling reporter for clarifications. Multiple reasons including lack of staff training were identified for near misses. Drugs most frequently involved in near misses were anti-infective [22.6%], cardiovascular [19.6%], and central nervous system [14.6%] agents. This study found some important tentative pharmacovigilance insights into near misses, which are comparable with current international trends in near misses/close calls and called for further studies on near misses in KSA [164]. Another study has analyzed the reported electronic prescribing near misses/close calls in KSMC, Riyadh, which were consecutively collected over a period of one year [year 2012]. The ME report forms were evaluated for data abstraction and a comparative analysis of NMs of first six-month (n=1025, timeline 1) versus second 6-month (n=2398, timeline 2) was carried out. No systematic intervention prior to

timeline 2 was used in this study [165]. The total number of reported NMs was 7415, as each form could contain more than one NM. Drug prescription items, medication dispensing stages, NM makers and identifiers, underlying causes, sites of errors, prescribed drugs and suggested actions to avoid NMs all differed significantly between the two timelines, which could be attributed to natural, real world practices in KSMC. This study called for more NMs comparative studies using systematic intervention in KSA [165].

3.14 E-prescribing Needs in KSA

Although Saudis accept the need for EP, its implementation across all health care delivery systems including the private sector has been minimal and slow, with only a few hospitals now having an EPS [160-161]. The problems associated with handwritten prescriptions need to be addressed globally. Major medical centers such as King Saud Medical City, King Fahad Medical City, King Abdulaziz Medical City, and major hospitals such King Fahd Hospital Dammam, and National Guard Hospitals have already implemented EHR that include electronic prescribing systems. The pace of implementing EHR with EPS has increased recently and 70 or more hospitals across the country now have fully functioning e-prescribing systems [162-163]. The present authors argue that the time is right for the Saudi Ministry of Health to develop a comprehensive plan for EPS implementation in all current and future hospitals in all 13 regions and urban PHC centers in KSA. EPSs will need to be implemented in rural PHC centers in phases. The private health sector should also be encouraged to implement EPS. Such an agenda would be in line with the recent rapid implementation of e-prescribing in Canada [166]. Limited research data suggest that there is a continuing need for further studies on EHRs and electronic prescribing in WHO-EMR countries.

4. DISCUSSION

As there is a significant amount of literature on electronic prescribing, it was not possible to include all studies in this narrative review. In addition, studies published in peer-reviewed international journals from the Eastern world are limited. This could be due to publication bias and/or, to a lesser extent, selection bias and non-exhaustive computer search of pertinent literature. Obviously, there are many search engines other than we used for retrieving relevant articles. Despite these caveats, this brief

narrative literature review strongly suggests that EPSs appear to be an invaluable component of health care systems and so have been implemented by almost all Western nations and upper to lower-middle income countries of the world. As EP involves an initial large capital investment, it might best be implemented in phases, first in academic centers, then in general/specialist hospitals, and finally in PHC setting and the private health sector. Notably, some countries have implemented EPS more than others, such as Australia, where 90% of pharmaceutical healthcare services are delivered through EHR and EPSs [75]. There is converging evidence that EPSs prevent certain types of MEs but add/facilitate other prescribing errors, especially omission and commission types [106,167]. These new errors have been attributed to several factors, including initial adoption of EP, overriding alerts, untrained electronic prescribers, limited functionality of EPSs, and the dispensers and prescribers of medication [41,46,71,105]. Since the implementation of EPSs, there have been continuous improvements and redesigns using HIT software. Furthermore medication prescribing suites, guidelines-based CDSSs, e-prescribing tool subscribing to the role of patients, and incentive schemes have been developed and incorporated into electronic health delivery systems that have increased the use of e-prescribing [36,168-170]. In addition, recently standards have also been developed for prescribers' transitioning to e-prescribing and for remote prescribing (telemedical e-prescribing) that could lead to safer medication management and hence greater patient safety [171-173].

Comprehensive EPSs and EHR embedded with CDSSs, DDI alerts, and other types of supports and alerts are reported to have many advantages. These include increases in patient safety and quality of life, patient and provider satisfaction, cost-effectiveness and reduction in the rate of MEs with time and system refinements [37,70,74-75,135,174-175]. However, EPSs/CPOE also have some disadvantages [8]. These include the inability to electronically prescribe controlled medications, professionals' tendency to override system alerts, inability to identify physicians who write incorrect prescriptions, facilitation of new types of MEs, a non-intuitive interface and incorrect dosage function, and the unfavorable perceptions of providers and/or their low levels of satisfaction [168-169,176-178]. For health technocrats, these and others are some of the

challenges such as use of formulary checks and medication history documentation [179]. Healthcare providers need comprehensive, fully functional EHRs integrated with EPSs that can capture all MEs, have workflow efficiency, and satisfy all stakeholders. EPSs need regular updating and may need redesigning in the future.

The landscape of EP is changing in mental health settings and more public mental health hospitals [180] and drug abuse treatment centers are adopting EPSs that deliver controlled drug e-prescriptions [181]. However, this changing scenario has highlighted some security issues and it remains to be seen how concerned health authorities and EPS developers will solve such legal issues by developing appropriate strategies and policies, which are of tremendous importance to both patients and health providers [8,181-182]. Furthermore, electronic pharmacopoeia is useful in guiding prescription of dangerous extended release and long acting opioids formulations by consistently providing their boxed warning information [183].

The studies included in this brief review have encompassed several significant topics, including several components of EP errors and processes; perceptions of prescribers, health consumers, pharmacists, and health managers; multiple settings including PHC, community, general and teaching hospitals; prescribing in pediatric and elderly population; the roles of CDSSs and DDI and other alerts; EPS related new types of errors attributed to multiple factors especially system failure and human factor; the cost-effectiveness of EP; the EP of controlled substances; outcomes of studies of EPSs; patient involvement in EP; pharmacists' interventions; computerized nurse order entry (NOE) and CPOE; MEs preventive strategies; applications of EHRs, EMRs and EP. Therefore, these studies are heterogeneous in their scope but compatible with diverse elements of electronic prescribing and related issues. These studies reported variable findings attributed to differences in methods and material, topic under consideration, and differing EPSs. Continuing community awareness programs, health providers' training, and consumer education and counseling are other important issues that tend to increase the acceptance and safety of electronic prescribing [8,184].

We predict that more data will emerge globally on EP in future and studies will especially focus on how to further improve EP through the

adoption of newer technologies to meet challenges, utilize opportunities, and further reduce the rate of EP errors via further strengthening of EHRs and EPSs. New implementers need to select an EPS that matches the needs of their health organizations and is compatible with their EPS plan, training perspective, investment, and implementation and evaluation processes. In addition, there are many EP research avenues open for those in the WHO-EMR countries through which to develop their own EPS knowledge base and meet the local needs of healthcare providers, consumers and health organizations.

5. CONCLUSION

EPSs are powerful troubleshooting tools in the hands of health care providers with which to positively affect the outcome of medication electronic prescribing by reducing EP errors, enhancing safety and quality for patients, increasing the satisfaction of all stakeholders, saving costs, and decreasing morbidity and mortality. The safe prescription of medication in a cost-effective way is a noble goal of all health providers that is also desired by patients. Electronic health records with EPS integration and other support systems such as CDSS collectively can contribute to achieving this goal.

6. KEY POINTS

- There is converging evidence that EP supported by CDSSs results in legible, complete e-prescriptions, considerably reduces serious MEs, increases workflow, efficiency, quality of healthcare services and patients' safety, enhances health providers' and consumers' satisfaction, saves time and costs, and also decreases overall morbidity and mortality.
- The initial implementation of EPSs with multiple support systems has challenges, variable outcomes and risk-benefit ratios, high cost, and health care providers have extensive training needs. As there are obviously variations in health care systems in WHO EMR countries, these factors need to be considered by a country prior to the adoption of an EPS.
- Although EPSs reduce MEs, they may also cause a variety of new MEs. In addition, a minority of physicians tends to resist EP and feel frustrated by its use. Hence, preventive strategies against these barriers

and felicitation of new types of errors, such as redesigning and regular updating of EPSs and incentives together with fewer drop-down menu selections should be implemented. The policy recommendations should include the emphasis on adopting EP for ensuring quality healthcare, patient safety, reduction in MEs, need for investment, training, technology, and change management.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

COMPETING INTEREST

Authors have declared that no competing interests exist.

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