ABSTRACT Unlike sub-optimal prescribing, rational prescribing, coupled with certain indicators, is associated with improved safety in drug use in terms of selecting appropriate drug for prescribing, better quality of life for patients and cost-effective care. Medication prescribing is a relatively unexplored area of research in Saudi Arabia and until now most studies have been in the secondary and tertiary health care system. This paper is the second of 3 review articles that form the background for a series of 5 interconnected studies of prescribing patterns and medication errors in the public and private primary health care sectors of Saudi Arabia. A MEDLINE search was conducted to identify papers published in peer-reviewed journals over the previous 3 decades. The paper reviews rational prescribing with its indicators, suboptimal prescribing, classification of medication errors, and how to achieve quality in health care prescribing worldwide and in Saudi Arabia.
Introduction

Rational prescribing by physicians is often described as an absence of irrational prescribing; in other words, it is easier given our current state of knowledge to define what is bad prescribing of medications rather than what is good prescribing. Bad prescribing can be defined by any number of indicators: the prescribing of an excessive range of drugs, the underuse of effective drugs, the overuse of drugs of limited clinical value, not prescribing drugs by generic name, and so on.

Most existing indicators for assessing rational prescribing focus on the cost of medications or the choice of drugs; others focus on quality of care, as noted in documents that emphasize the process of prescribing [1]. The UK Audit Commission defined rational prescribing as low-cost prescribing, while acknowledging that there may be valid reasons for higher cost prescribing at times [2]. Avery reviewed the many attempts to derive simple formulae to interpret prescribing from the UK’s prescribing analysis and cost tabulation (PACT) data and concluded that existing prescribing indicators included few of the key attributes of rational prescribing and could not be used as management tools for monitoring rational prescribing [3,4].

Physicians’ views of what is rational prescribing tend to focus less on the choice of drug and more on the appropriateness of the drug. Parish described it as the prescription of drugs that were: appropriate, safe, effective and the least expensive for the purpose [5]. Bradley noted that there was a lack of empirical evidence on how best to judge quality in prescribing and favoured a definition that involved balancing the evidence about the most effective way to treat a medical condition against the associated costs [6]. Barber updated the Parish definition by criticizing its focus on the prescriber and on managerial control of over-prescribing and its costs. He acknowledged that the various domains of what might be called good prescribing—maximizing effectiveness, minimizing risks, minimizing costs and respecting patient choice—could conflict with one another [7]. Good prescribing then becomes a balancing act of these domains and this model replicates the key elements of medical ethics: beneficence, nonmaleficence, distributive justice and autonomy [8].

Another professional view of rational prescribing was presented by Marinker and Reilly, who argued that it can only occur in the context of rational management of the patient, rational diagnosis etc., and therefore cannot be determined from crude data such as PACT [9]. Rational prescribing starts with a rational formulation of the patient’s problem, especially a rational diagnosis, i.e. one that is defensible and can be confidently supported by evidence. This provides clarity of therapeutic intention on behalf of the prescriber. Rational prescribing also inherently has a time dimension: choosing the optimum point to initiate the therapy, the optimum duration of therapy and the optimum point to stop the medication. Rational prescribing requires not only control mechanisms that encourage compliance but also educational activities that encourage an active process of judging the appropriateness of the diagnosis and the therapy. Rational prescribing also needs to be judged on the basis of the complex interactions that take place in the consultation. PACT data alone can identify certain aspects of irrational prescribing, but are limited. Detailed medical audit on a case-by-case basis gets closest to the patient’s actual complaint and the optimum treatment for it and this may be the best we can do in systems of clinical governance.

In developing countries, rational prescribing may be defined by what can realistically be measured. The World Health Organization (WHO) defined rational prescribing as “the 5 rights”: the right drug, right dose, right route, right time and right patient [10]. This definition may be criticized since it assumes a clear diagnosis of the patient’s problem rather than a “best formulation” of care as in the UK models of rational prescribing. Nevertheless, it is reasonable that both a clear diagnosis and a formal treatment plan should be the foundations of rational prescribing.

Compared with more industrialized countries there are few studies from Gulf countries that explore rational prescribing. This paper is the second of 3 review articles that form the background for a series of 5 interconnected studies of prescribing patterns and medication errors in the public and private primary health care sectors of Saudi Arabia [11–15].

Indicators for rational prescribing

A key definition of rational prescribing must rest on what can actually be measured. Two measures are commonly used: the medication appropriateness index (MAI), developed by Hanlon et al. [16] and the prescribing appropriateness indicators (PAI), developed by Cantrill et al. to assess long-term prescribing [1]. They are similar in content and considered by some commentators to put too much emphasis on the pharmacological aspects of prescribing [17]. The key elements are: indications; effectiveness; dosage; directions; drug interactions; drug–disease interactions; expense; practicality; duplication; and duration [18]. The UK the Audit Commission’s definition of rational prescribing, which focused on costs [2], has been controversial. WHO produced a list of 12 external indicators under 3 headings—prescribing, patient care, facility [19]. While these may help in assessing prescribing by individual physicians the value of the data are hampered by their widely divergence across developed and developing countries.
Prescribing and drug choice

A key aspect of rational prescribing is the choice of drug(s) (assuming that both doctor and patient have decided a drug is necessary). This might seem to be a simple decision using evidence-based medicine, but is in fact more complex [20]. The main factors that a physician needs to take account of when choosing a drug have been defined as: evidence of effectiveness and safety; tolerability; compliance; ease of prescription; supply; and cost [21]. These doctor–drug factors, however, are compounded by influences from patients, other doctors and professional sources, pharmaceutical companies, government and health insurers, mass media and personal experience. Physicians use negotiations with the patient, consultations with other physicians working in hospitals and primary health care and proper scrutiny of pharmaceutical information to reduce these pressures.

Physicians prescribe from a personal drugs set or formulary. They may prescribe new drugs either as a one-off or to allow them to reshape their personal drug set. This personal set is in part formed during early medical training and then modified by all of the influences outlined above, especially by personal experience. The formulary may also be shaped by external forces, e.g. imposed by the government, as occurs in publicly-funded care in Saudi Arabia and elsewhere, or by insurance schemes in the USA. While a physician’s prescribing behaviour tends to default back to the personal, he/she must always question whether the drug is right for each patient. WHO have a well-developed teaching system for medical students around the establishment of a “P (personal) drug” set and the decision about whether a drug is appropriate for an individual patient [19]. This scheme was used later in a modified form as an intervention to try to bring about changes in prescribing behaviour. In practice, doctors adopt a range of short cuts and rules of thumb to make the process of selecting a drug faster and easier. Such decision-making shortcuts represent a variety of decision-making strategies for prescribing which combine pragmatic, analytic, intuitive and emotional influences [20].

Decision-making in prescribing is a dynamic, complex process. Decision analysis has been defined as comprising 5 steps [22]: define the problem and the objectives; structure the decision-making problem; identify all possible alternatives and relevant criteria; estimate the probability that a particular option will lead to a specific outcome; evaluate the benefits of each possible outcome; and choose the best option by combining probabilities. In addition to these steps, for prescribing decisions we could add the need for monitoring (step 6), feedback (step 7) and corrective action (step 8).

Achieving quality in health care

Both the providers and consumers of health care can contribute to improving the quality of services and hence patient quality of life by setting standards. Excellent quality health services must address the needs not only of those who need the service most but also those who need it least [23,24]. Currently, in Saudi Arabia people with sufficient funds have access to both public and privately funded health care; those who do not have access only to publicly funded health care. Arguably health services should focus on the poor rather than the rich and any element of cost should not discriminate, since the poorer sectors of the community tend to suffer the greatest morbidity and hence have more treatment needs. Not all countries follow with this fundamental principle, e.g. in the US, where ability to pay is still the key to access to high quality services. Most publicly funded health services in Europe, however, do subscribe to this approach, as do those in wealthier developing countries. Poorer developing countries in contrast often have to introduce user charges which limit access to care. Cost is almost always an issue in every country [25]. As a result, the best possible quality of services should be delivered within the limits and directives set by higher authorities, usually governments, although this does not exclude exceptional requests for greater funding from health professionals, health providers and health consumers.

Two complementary approaches to promote the quality of health care have been developed [26,27]. First there is the development and use of benchmarking to generate standards and targets against which the performance of health care providers can be evaluated. The second approach is to evaluate the quality of the services from the perspective of the ultimate consumer of the service: the patient. Quality assurance in health care should have a sound foundation in terms of the health system design, coupled with continuing performance assessment that should lead to appropriate educational–motivational activities and refinements in the system design, either in performance or standards or both [28]. Furthermore, quality assurance should deal with the real health problems of consumers and communities within the limits of the available resources and assess different outcomes with the goal of satisfying patients [26,29,30] and evaluating patient care safety [31].

Achieving quality in prescribing

Educational and information approaches

One approach to improving quality in practice is educating doctors to change their behaviour. A Cochrane review of the effects of continuing education on professional practice and health care
outcomes concluded that interactive workshops could result in moderately large changes in professional practice, whereas didactic sessions alone were unlikely to be effective [32].

A study by Allery et al. involving 50 general practitioners (GPs) and 50 consultants sought to describe the complete range of factors that doctors recognize as changing their clinical practice and to provide a measure of how often education is involved in change [33]. The 3 most frequently mentioned reasons for changes in clinical practice were: organizational factors; education; and contact with professionals. Consultants stated that they were influenced by medical journals and scientific conferences, while GPs thought they were more influenced by medical newspapers and postgraduate meetings. The authors concluded that education is involved in about a third of changes in professional practice [34].

Cantillon and Jones's review of the literature summarized the effectiveness of continuing medical education (CME) in the context of UK general practice [35]. This review indicated that the most effective methods for bringing about change in GPs’ behaviour were: learning linked to clinical practice; interactive educational meetings; outreach events; and strategies that involve multiple educational interventions. The authors noted that the least effective methods for CME were those most commonly used in general practice.

Soumerai and Lipton critically reviewed the available evidence on drug information bulletins, guidelines and other professionally prepared materials. They observed that printed materials on their own generally have limited, or no, effectiveness in influencing changes in prescribing behaviour and that any noticeable effect was usually short-term [36]; similar conclusions were reached in a Cochrane review [37].

Educational outreach visits, however, can have an effect on prescribing behaviour, particularly when combined with social marketing related to a socially beneficial change [32]. This is the basis of the system of visits by prescribing advisers in the UK [8]. However, educational outreach was associated with only a 7% increase in the desired professional practice [38,39].

Administrative approaches

Administrative approaches can also be used to improve quality in practice [40]. Examples include incentive schemes such as the GP fund-holding scheme in the UK [41,42], in which changes in prescribing practice, albeit limited in magnitude and sustainability, were achieved by simple measures, e.g. introducing generic prescribing [41]. The opposite of providing incentives is to provide disincentives, as attempted in France and in Germany. These have achieved mixed results and engendered considerable dissatisfaction from doctors.

Another aspect to the administrative approach is providing feedback to doctors on their prescribing habits. Harris et al. described this as a powerful but transient approach to changing prescribing practice that can only succeed if there are professional incentives [43,44]. The feedback approach can be useful as part of a multifaceted approach to achieving changes in professional practice [45].

Even if prescribing can be improved by educational methods and to a lesser extent by managerial actions, these approaches are more likely to be influential on what drugs are prescribed rather than on whether a drug needs to be prescribed at all. Formularies are a good example of this [8]. Clinical guidelines may also be effective and might bring about greater changes, but only if they are acceptable to the profession [38]. In future, computerized decision support systems may be the most useful tool [8], but these are unlikely to be implemented in Saudi Arabia in the near future. Better quality prescribing in Saudi Arabia may be as simple as encouraging proper documentation of prescriptions.

The need to improve patient safety by reducing prescribing errors and adverse drugs events (ADEs) has been increasingly recognized by the medical community. This concern was highlighted after the publication of recommendations from the Institute of Medicine [46] which were supported by other investigators [47,48]. These focused on enhancing the knowledge base about safety; identifying and learning from errors; raising standards and expectations for improvements in safety; and creating safety systems inside health care organizations. Besides the domains of patient safety and organization assessment tools, the Institute rightly identified the roles of the public, the media and stakeholders from different disciplines.

Grube has commented about the deficiencies in the reporting of prescribing errors and identified barriers to reporting errors—e.g. physician’s fears of legal vulnerability, the culture of health care providers and an organization’s unwillingness to take corrective action—together with possible solutions [47]. In the UK, the National Patient Safety Agency has been set up to address system errors in drug prescribing and medication use, and a target was set to
reduce the number of serious errors by 40% by the year 2005. This may be difficult in the UK where the rate of medication errors was reported in one hospital to be 3.0%, significantly lower than the rate of 6.9% reported in a US hospital with a typical unit dose drug distribution system [49].

Categorizing suboptimal prescribing

In any analysis of suboptimal prescribing, it is crucial to distinguish clearly between prescribing errors, dispensing errors and ADEs. Notably, accurate definition of the prescribing problems being addressed is crucial to the development of effective solutions.

A number of terms are used in defining suboptimal prescribing. The term “patient safety incident” is an umbrella term to describe a single incident or a series of incidents that occur over time [50] and is preferred to the terms “adverse event”, “clinical error” or “near miss”, as such terms suggest individual causality and blame. The concept of “trigger data” has been developed to reflect the use of clinical data which indicates the probability of an ADE developing. For example, a medication, laboratory value or other indicator that indicates the probability of an ADE or ADEs rarely have single causes and the doctrine of causation is used to relate a range of factors including predisposing, enabling, precipitating or reinforcing factors to the occurrence of such events [51]. It is important, therefore, to investigate a wide range of factors in suboptimal prescribing. Each contributing factor represents an active failure, such as a situational factor or a latent condition that played a role in the suboptimal outcome [51]. In addressing suboptimal prescribing, it is essential that a culture of safety is encouraged throughout the whole organization.

This requires the development of an integrated pattern of individual and organizational behaviour that continuously seeks to minimize any form of patient harm resulting from care [52]. “Dispensing errors” are a deviation from an interpretable written prescription or medication order, including written modification of the prescription made by a pharmacist following contact with the prescriber or in compliance with the pharmacy policy. Any deviation from professional or regulatory references, or guidelines affecting dispensing procedures, would also be defined as representing a dispensing error [53].

A “drug-related problem” is defined as an event or circumstance that actually or potentially interferes with the desired health outcomes arising from drug therapy [54] and adversely affects the benefit–risk ratio for an individual patient. “Prescribing errors” take many forms: a drug at the wrong time, administering it in the wrong dosage or administering it by the wrong route. An error of omission occurs when an ADE results from an action not taken; for example, when a dose of a medication should be administered but is omitted [55]. Failure mode and effects analysis (FMEA) is a risk assessment method based on the simultaneous analysis of failures modes, their consequences and their associated factors and is used to attempt to identify and prevent problems before they occur. A wide range of alternative risk assessment methods using the failure mode technique exist, all of which assume that prescribing errors are inevitable and that the aim must be to identify systems by which such errors can be minimized. A “just” culture is a key element of a “safe” culture that reconciles professional accountability within a system which balances the need to learn from mistakes and the need for disciplinary action [56]. A just culture hinges on a collectively agreed and clearly understood distinction being drawn between acceptable and unacceptable behaviour [57]. Marx has expanded the concept further and provided practical guidance on its use in health care organizations [56]. “Error conditions” are defined as errors in design, organization, training or maintenance that may lie dormant in systems for long periods of time [46]. Unlike active failures, latent conditions can be identified and remedied before an ADE occurs, enabling proactive rather than reactive risk management [58]. Latent errors have been described as “accidents waiting to happen” [59] and can translate into error-provoking conditions within the local workplace or long-lasting weaknesses in the defences of the system.

A “medication error” can be defined as any preventable event that leads to inappropriate medication use while the medication is in the control of the health care provider or consumer. The medication use system represents a combination of interdependent processes: selecting and procuring; storage; prescribing; transcribing and verifying; preparing and dispensing; administering and monitoring [60]. Each major process presents its own unique opportunities for error [61]. A “monitoring error” occurs as a result of failure to review a prescribed regimen for appropriateness and for detecting problems, or failure to use the appropriate clinical or laboratory data for adequate assessment of the patient response to the prescribed therapy. An “opportunity for error” is the basic unit of data in medication error studies and is defined as any dose or doses given, plus any dose ordered but omitted [62,63].

Taxonomy of medication errors

Not all ADEs are due to prescribing errors. There are many types of clinical errors with multiple etiologies. There are also several taxonomies of medication errors and a number of authors have
described different ways of classifying clinical and prescribing errors.

- Clinical importance of the event. Neville et al. classified clinical errors into 4 major groups: type A are potentially serious to patients; type B are a major nuisance that require contact between the pharmacist and prescribing doctor for clarification; type C are a minor nuisance where the pharmacist must use his/her professional judgement when dispensing; and type D are trivial [64].

- Dispensing errors. Ross et al. in a study of a paediatric hospital have classified medication errors, largely dispensing errors, into 8 types: wrong medication; wrong dose of medication; wrong concentration of medication; wrong fluid or wrong rate of injecting medication; medication administered at a very different time from when it was prescribed; medication likely to produce a known allergic reaction; medication given but not prescribed or vice versa; wrongly labeled and wrong medicine or strength of medicine dispensed for use at home. [65].

- Effectiveness and safety or cost-effectiveness. Soumerai and Lipton highlighted common prescribing errors in terms of: use of toxic or addictive drugs when safer agents are available; use of drug therapy when no therapy is required; use of an ineffective drug; use of a costly drug when a less expensive preparation would be just as effective; suboptimal or excessive use of effective agents; failure to discontinue therapy when the drug is no longer needed; and failure to introduce new and effective drugs into practice. This might be extended to include any under-use of an effective drug [36].

- Health care quality problems. The IOM developed the approach of Soumerai and Lipton [36] and described 3 types of health care quality problems and prescribing errors—under-use, overuse, misuse—all of which need to be addressed to improve patient safety [66,67]. Reported misuse is closer to what Neville et al. and Ross et al. recognize in terms of actually making an error, e.g. prescribing the wrong drug or dose [64,65].

- Pharmacy errors. Kelly, after reviewing 17 studies discussed the contribution of the hospital pharmacy to preventing or causing ADEs and classified pharmacy errors into the following: errors due to system failure; errors due to insufficient supervision or staffing; and errors by pharmacy personnel [68].

- Allergies or interactions. Rozich and Resar documented several types of medication errors, including allergies or interactions: errors related to drug, dose, drug administration; medication administration records; allergy or interactions; and others [69].

- Psychological. Other researchers have given a psychological classification of medication errors, drawn not from the prescribing literature but more broadly from the literature of industrial safety [70]. Such mistakes include knowledge-based and role-based errors: mistakenly applying a good rule, e.g. injecting anti-inflammatory drug diclofenac into the lateral thigh (the usually preferred site) rather than the buttock (which is recommended for diclofenac); or applying a bad rule, e.g. when excessive doses of the ACE inhibitor captopril were used when it was first introduced.

- Underlying cause. Dovey et al. undertook a detailed analysis of medical errors in family practice [71]. Errors were categorized in relation to their underlying cause, primarily as due to problems with processes involved in carrying out general practice and skills involved in general practice.

Although the adopted taxonomy of prescribing errors certainly differ across studies, all of them to some extent help in identifying the causes of errors and methods to reduce them. Both prescribing errors and ADEs are preventable and need proper investigation by the relevant authorities using standardized protocols.

In summary, rational medication prescribing is closely linked with patient safety and quality of life. Suboptimal prescribing, especially medication errors, are classified variously by different researchers. The common theme, however, is the need to identify the causes out of the range of possibilities and to create practical systems for preventing them.

References


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**The International Pharmacopoeia**

*The International Pharmacopoeia* (Ph. Int.) comprises a collection of quality specifications for pharmaceutical substances (active ingredients and excipients) and dosage forms together with supporting general methods of analysis, that is intended to serve as source material for reference or adaptation by any WHO Member State wishing to establish pharmaceutical requirements.

The activities related to *The International Pharmacopoeia* are an essential element in the overall quality control and assurance of pharmaceuticals contributing to the safety and efficacy of medicines. The selection of monographs for inclusion in *The International Pharmacopoeia* recognizes the needs of specific disease programmes and the essential medicines nominated under these programmes; it is based primarily on those substances included in the current WHO Model List of Essential Medicines.

The Pharmacopoeia and related documents can be downloaded from: