

Generic Prescribing: The Egyptian semblance

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Abstract

Generic prescribing is prescribing medicines by the prescriber using the international non-proprietary name, leaving the choice to the pharmacist to either dispense the brand or its generic counterpart. Generic prescribing allows any suitable generic drug rather than a brand drug to be dispensed, reduces delays in supplying medicines to the patient and leads to cost savings. Several countries have issued regulatory policies for the use of generic medicines to facilitate the access of medicines and for cost savings purpose to decrease the rapid growth of spending in the healthcare system. The aim of this current review is to highlight the current status of generic prescribing and prescribing practices in Egypt, regulatory policies as well as the perceptions of the physicians, pharmacists and patients' towards generic prescribing and its economic impact.

Key words

Generic prescribing, Physicians, Pharmacists, Patients, Egypt

Medicines prescribing

Medicines prescribing includes all the process incorporated in decision making in which the prescriber performs before writing a prescription. Only medical, dental or veterinary professionals were authorized for prescribing in the past but now days the right of prescribing have been extended in some countries to other healthcare professions including pharmacists and nurses [1]. Independent prescribing is defined as prescribing by the doctor, dentist, nurse or pharmacist who is in charge for the assessment of either diagnosed or undiagnosed patient and for making decisions regarding the required management including prescribing. In 2006, pharmacists were able to prescribe only licensed medicines for any medical conditions but were not able to prescribe any controlled drug or non-licensed medication, however in 2010, they were allowed to prescribe unlicensed medications [1, 2]. The prescribing process includes consultation which is the most crucial part in prescribing, based on identifying the reason for patient consultation, gathering information related to the patient problem, physical examination, explanation and making decision together with the patient. Secondly, communicating and explaining the benefits and the risk of the treatment and ensuring patient adherence to the treatment [3].

Many factors can influence the prescriber during making the decision when prescribing medicines. Besides the clinical, cost effectiveness and appropriateness of the medicines, the pharmaceutical industry [company advertisements and representatives] plays a critical role in drug prescribing; as pharmaceutical companies regulate regular contacts with physicians through pharmaceutical sales representatives who visit physicians at least once weekly [4, 5]. Information sources can also influence the prescribing of medicines, for instance, academic sources as scientific journals, conferences and

magazines through scientific articles and talks were rated as a very important influencer in the prescribing of drugs, especially for new drugs [6]. Among the other factors are the national healthcare policy, guidelines and local formularies. The prescriber also trusted colleagues including the hospital specialist in case of primary care, pharmacists in the primary and secondary care [7, 8]. Drug samples which are widely available in clinics can affect the prescribing behaviour of physicians. Interestingly, these drug samples are more acceptable for physicians than personal gifts, however after running out of the drug samples, physicians prefer writing the same sample drugs in their prescriptions [9]. Patients and the culture can influence the prescriber behaviour, as many patients demand prescription not only for its therapeutic activity but also to demonstrate that their illness is recognized or just to fit with their health beliefs and sometimes to get time off work for their illness. Media which are directly advertise medicines to patients also play a role as patients exert pressure on the prescriber for a specific medicine [8].

Rational use of medicines

The rational use of medicines is the appropriate use of medications when there is an evidence-based indication, cost effective in the proper doses and period of time [10]. From the point of view of a consumer, the rational use of medicines is the perception of drug value in daily life from the economic and culture perspectives [11]. According to Barber framework of good prescribing, the prescriber should aim to achieve maximum efficacy, the least risk, minimum cost and recognize the patient choices [12]. Another a framework of prescribing decision proposed by Preskorn is known as "STEPS" which means safety, tolerability, effectiveness, price and simplicity [13].

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Good prescribing can also be defined as the lack of irrational prescribing which includes poor medicine choice, polypharmacy and prescribing of interacting medicines, use of expensive or drugs not related to the diagnosis, misuse of antibiotics, inappropriate doses, prescribing without sharing decision with patients, prescribing medication for a self-limited condition and prescribing for unnecessary long period of time. Irrational prescribing is a worldwide issue that can cause morbidity and mortality especially in children and patients with chronic diseases like hypertension, diabetes and heart diseases. The problem also exacerbated because of dispensing a large proportion of drugs in the private sector without prescription [8, 14].

Self-medication is a common practice among patients worldwide in both developed and developing countries, where medications can be easily be obtained over-the-counter from the pharmacy or drug shops which can result in a serious public health problem [15, 16]. Most common reasons towards self-medication was to treat minor illness, avoid long waiting periods in hospitals and save money. The mainstay of the misuse of medications is over-prescription and self-prescription of medicines [17]. Egypt is among the highest in the world for per capita use of prescription medicines [18, 19]. Self-prescription is also common in Egypt, because medicines can be dispensed without prescriptions.

Several actions are recommended to rationalize the drug use through rational prescribing by applying standard guidelines for treatment, essential drug list [EDL], establish a pharmacy and therapeutics committees to monitor medicines use in hospitals, promote continuous education programmes through printed materials, seminars and direct interventions by professional universities [20]. Also restrictions on prescribing that include restrictive lists, the maximum number of drugs per prescription, cost restriction, price measures and strategies for patients co-payment is recommended [14]. A pilot baseline situational analysis performed in Egypt showed that although 16.07% is only the mean percentage of drug prescribed in generic name and 50% in the primary healthcare centres, generic name prescribing aid in rationalizing the medicines use and help in decreasing the economic burden on the individual [21]. Prescribing medicines using a generic name may reduce duplicity, facilitate access to drugs and improve patients' compliance with the drug and then controlling disease according to a study performed in university-affiliated outpatients clinics in South and Mideast of Brazil, in which generic name prescribing represent 86.1% of total prescribed drugs [22].

Generic medicines prescribing

Generic medicines prescribing is using the generic name [international non-proprietary name] of the drug rather than the proprietary name when prescribing it by the physician. This allows the pharmacist to choose either to dispense the branded or the unbranded [generic medicines]. It completely differs from the generic substitution of the drug in which the pharmacist is the initiative by dispensing different branded or unbranded medications instead of that written by the physician. This substitution includes the same chemical entity of the drug also the same dosage form but different companies [23]. After the expiration of branded-name drug patency, generic medicines products can be produced. The FDA publishes a list of the patent expired brand-names then other manufacturing companies can get approval to market generic versions of these branded-name drugs [24].

The FDA defined generic medicines as drug product that is comparable [copies] to the brand-name drug products in strength, dosage form, quality, safety, route of administration and performance. Whereas, the European Medicine Agency [EMA] defined the generic medicine as a medicine which is developed to be the same as the authorized medicine. Generic medicines contain the same active ingredient as reference medicine, used at the same dose to treat the same disease as the reference medicine however the name, appearance [colour, shape] and packaging is different from the reference medicine [25].

The FDA approves the generic counterpart of a medicine after certain measures. The generic manufacturer must perform bioequivalence studies that included at least 40 healthy individuals to prove that the generic medicine has the same pharmacokinetics profile as the brand-name counterpart. A deviation in confidence interval from 80-125% between the branded and generic name counterpart is acceptable, however in certain indications as in epilepsy and some hormonal replacement therapy, it is not recommended to substitute brand-name with generic medicines owing to the lack in bioequivalence between both of them [26]. Generic medicines should also have the same indication, being bioequivalent and having the same batch requirement as for the quality, purity and strength [25]. The FDA ensures the presence of good manufacturing practice regulations [GMP] during the manufacturing process. Any differences must be restricted to the packaging, storing conditions, tablet shape and drug excipients; colour, preservative and flavour.[27, 28].

Generic drugs have a crucial role as a branded-name as drug alternatives in the management of several diseases. Having the same qualitative and quantitative composition of the active constituents, the same dose, the same dosage form, the same route of administration, the same bioavailability, the same quality and the same stability; generic drugs are considered bioequivalent to brand-name counterpart drugs. Any differences must be limited to the inactive ingredients like fillers, colouring, flavouring, stabilizing agents and packaging. For these reasons, generic drugs are supposed to have similar therapeutic efficacy and safety profile to the branded-name drugs [29].

The difference between the generic and the brand-name drugs is that the brand-name drugs are manufactured and supplied from one company and sold under a trade name however the generic drug can be manufactured by many companies and sold under names of active ingredients [28]. The originator product [brand-name] is the product that authorized in a country to be the market for the first time. This product gains its patency based on the efficacy, safety and quality [30]. The unbranded or generic products are off-patent, non-originator products that marketed under an international non-proprietary name; INN [the name of the ingredient molecule] not the brand-name or trade name.

Generic medicines marketing authorisation and generic pricing

Generic medicines authorisation according to EU and US legislations permit the use of abbreviated application in which preclinical and clinical studies are not included for enhancing the price difference between the generic and the brand-name medicine [25]. In lower- and middle-income countries, there is a difficulty in promoting the use of generic medicines due to the absence of generic substitution regulations and policies, the lengthier time period needed for marketing authorisation and lack of transparency in the pharmaceutical supply and distribution system and negative perceptions of stakeholders

[31]. For example, the generic drug needs from 6 to 8 months for market authorization however the originator market authorisation takes from 8 to 14 months same as in Colombia [3 months versus 6 months] while lowering the marketing authorization fees is applied in Argentina and Chile [32]. Another policy in some countries such as Mexico, it is permitted the development of generic version by the generic manufactures before the patency expiry of the medicine in order to carry on any studies and tests until the patency of the medicine is expired.

Several policies were applied to regulate the pricing of the generic medicines in most countries. For instance, the pricing of generic medicine is set to be relative to the branded medicine. Generic drugs can be sold up to 60% less than the brand-name drugs in many European countries as in France [50%], Ireland and Greece [20%] [33, 34]. Reference pricing which is classified in internal reference pricing and external reference pricing. For internal reference pricing system, drugs are classified into reference groups in which each group include drugs usually off patent or alternative medicines with similar or identical active ingredients within the country, then the maximum reference price is determined for each reference group taking into account the prices of medicines that are already in the other reference groups [35]. It has been noted that about 32% of European countries depend on the lowest-priced medicine while 16% of them was dependent on the lowest-priced generic drug [36]. On the other hand, the external pricing reference compares drugs prices to patent medicines among countries. Some European countries as in Bulgaria and Poland use this system for off-patent medicine pricing [37]. In Europe, the generic pricing mainly affected by the competition with the Indian generic medicines manufacturers owing to the low cost of production costs and weak patent protection laws and this put pressure on generic medicines. Studies have shown that UK, Germany, Netherlands and France are the highest in prices of generic medicines because of depending on the discounting to the distribution chain rather than price competition [38].

Regulations of generic prescribing

The regulatory obligations of generic prescription is important, despite the differences in prescribing behaviour of the physicians towards brand-name and generic drugs prescription. The generic prescription depends on many factors including the different diagnoses, marketing and promotion policies, prescribing's behavior of physicians and also reflects the preferences and requests of the patients. Significant differences exist among the prescribing behavior of general practitioners for brand-name and generic drugs, these may create problems because of adverse effects on the cost of healthcare services and local economy that leads to different methods of controlling or sharing costs such as copayments and incentives to use generic alternatives [39, 40]

Some countries work on increasing trust regarding the quality of generic prescribing. European countries have set many financial and non-financial incentives to encourage generic prescribing [41]. Of these regulations to control prescribing costs and improve quality of care are implemented included the use of financial incentives for prescribers through increased financial accountability using drug budgets and performance-based payments. Physicians budgets seem also to encourage generic prescribing when rewards/sanctions are applied to compliance/non-compliance with budgets. In a study evaluating the effects of financial incentives for prescribers from the UK,

Ireland and Germany indicated increased use of generic drugs in the UK and Ireland, but was inconclusive on the use of new and expensive drugs; in addition drug expenditure [per item and per patient] and prescribed drug volume decreased with budgets in all three countries [42]. The national drug policies require all physicians in Latin American countries such as Argentina, Bolivia, Peru and Uruguay to write prescriptions using the international non-proprietary names [INNs], and also the regulations in Mexico and Brazil is oriented towards demonstration of the therapeutic equivalence of the generic medicines [32].

Many countries promote the use of electronic prescribing systems, prescribing guidelines and formularies, medicines databases in addition to performing pharmacotherapeutic discussions between physicians and pharmacists, in addition to encourage physicians to prescribe medications by their international non-proprietary name [INN] especially which have generic equivalents. Most European countries allow generic substitution by the pharmacist, where 71% of the European countries allowed generic substitution by the pharmacist who either free or obliged to substitute the prescribed drug by the physician to a less expensive one [41]. Generic substitution was adopted in countries where physicians are not adhering to generic prescribing, however some rules vary from one country to another that control dispensing in pharmacies as in 89% of countries physician can prevent drug substitution through ticking a box or writing on the prescription [35]. In Netherlands, pharmacists were encouraged for generic substitution by retaining 33% of the difference between the reference price and medicine price [41]. Dutch pharmaceutical policies promote incentives to pharmacies in the form of a fee that is equal to the difference in prices between the originator drugs and the generic drugs to enhance drug substitution. On the other hand, French pharmacists were encouraged to dispense generic medicines after declining the permitted mark-up for higher price drugs so the pharmacy mark-up is separated from the price of the prescribed drug [43].

The establishment of reference price can influence the demand for generic medications as the brand-name price is above the reference price level so the patient will pay the difference between the prices and the reference price [41, 44]. Some European countries encourage generic prescribing by removing medicines from reimbursement list or by restricting prescribing of some drugs, this was the case in Finland and Norway on switching from branded statin to generic statin [45].

Regulations of generic prescribing in Egypt

Medicines in Egypt are government-regulated and drug pricing is controlled by law and ministerial decrees. The newly founded regulatory body; Egyptian Drug Authority [EDA] is the pharmaceutical regulatory body responsible for the registration and pricing of medicines [46]. Previously, the Central Administration of Pharmaceutical Affairs [CAPA] under the ministry of health was responsible for registration, pricing, inspection, controlling, importation and exportation of pharmaceuticals. In 2009, a "box system" registration policy [ministerial decree 296/2009] was introduced to regulate medicines registration but recently the ministerial decree [425/2015] was issued that entails the maximum number of pharmaceuticals with similar active ingredients and product specifications is 12, including the brand-name. The "box system" registration is composed of similar products in certain dosage form of any active ingredient; one branded and 11

generic products [10 locally manufactured and 1 imported]. The latter ministerial decree [425/2015] enhances the registration period through allowing parallel pathway instead of consecutive approval [47]. The average timeframe for obtaining a marketing authorization is about 1-2 years. Registration of pharmaceuticals that are not registered in the country of origin or any reference country is more complex and lengthy. The marketing authorization is granted for ten years. The registration procedures for biological products do not differ much from the registration of other pharmaceuticals, and the marketing authorization is five years.

Medicines are registered either by the international nonproprietary name [INN] or the brand name and registration requires paying a fee based on the application; new chemical entity or generic pharmaceuticals [48]. Generic products which are either imported or locally produced, are subjected to markdown percentage from the original product reaches [35%] for the first five generic drugs that apply for pricing while the percentage reaches [40%] for the rest of generic drugs according to the pricing ministerial decree [499/2012]. In the case of the imported generic products, the markdown percentage is 30% and 35% of the branded name in reference and non-reference countries respectively [49]. Therefore, within a "box", the pricing committee rely on observing the descending prices of the generic medicines based on the registration date, in other words, the later the registration date the lower the price which is given to the generic medicine. Not all registered products can be marketed especially if generic medicines priced in low prices that not satisfy the manufacturer [49]. In 2012, the pricing policy changed and accordingly 206 products were subjected to pricing change, 70% of them were generic drugs [50]. Despite there are legal provisions that govern the prescribing practice in Egypt, but there is no strict policies or guidelines that regulate generic substitution during the dispensing process.

Factors affecting generic substitution

The selection and use of generic medicines in medical practice is influenced by many factors. These factors include physicians, pharmacists and patients' perceptions towards generic prescribing. The economic perspective and cost savings are also one of the reasons for introducing generic medicines.

1- Physicians' perspectives on generic substitution

Although physicians have a key role in choosing the medicines, physicians are affected by many determinants [51]. The physicians' decision can be influenced by patients' financial status, pharmaceutical company's advertisements, guidelines and their clinical experience. Several studies have reported that physician' medicines prescribing decision is attributed to drug efficacy, safety, quality, knowledge of guidelines, literature and clinical trials, clinical experience, patient affordability, patient clinical situation, contacts with pharmaceutical sales representatives and company advertisements and the trust and quality image of the pharmaceutical company [52-54]. de Run *et al.* reported that physicians' perception towards prescribing generic drugs is influenced by their uncertainty in the efficacy, safety and quality of the generic counterpart of the drug owing to the lack of clinical trials, but the majority of them adapt the cost-saving notion of the generic drugs [55]. In a Saudi study, regarding the physicians beliefs in generic medicines; the majority of physicians knew the therapeutic value of generic and the cost difference and [79%] of them supported the generic

substitution in most cases, but they preferred prescribing brand-name drugs in certain cases [56].

Paraponaris *et al.* surveyed general practitioners opinions regarding writing prescription by international non-proprietary name [INN] for three consecutive years and the analysis revealed that [76%] of respondents were willing to write prescription using international non-proprietary name [INN] but the study highlighted that meeting with medical representatives induced reluctance in prescribing medicines using international non-proprietary name; INN [57]. A study conducted in Iraq included physicians from different specialties revealed that [57.3%] of the respondents had negative perceptions regarding the quality and [41.1 %] regarding the safety generic version of the drugs compared to the brand-name drugs [58]. Although two third of the respondent were willing to prescribe low cost medicines, only half of them prescribe generic medicines, however [64%] of respondents didn't agree with the generic substitution in the pharmacy. Shrank *et al.*, reported that physicians had difficulties in medicines prescribing with more than half [51%] of their patients because of the prescription cost [59]. Although 67% of the physicians strongly agreed that there were no difference in efficacy between generic and brand-name drugs, many physicians, particularly those with an accumulating experience, were not confident regarding the quality of generic versions. They believed that patients overcame the cost by skipping doses to make the prescription stay longer or by taking smaller doses than the prescribed one to save money or even didn't buy the whole prescription.

Concerning the physician attitude towards prescribing generic drugs, especially those drugs with narrow therapeutic margins, Pereira *et al.* reported that [65%] of the respondents were generally agreed on prescribing generic medications but [44%] of them didn't agree with substituting brand-name with generic drugs as warfarin and [44%] of them preferred prescribing other anticoagulant agents instead of the generic warfarin [60]. Another study has demonstrated that some Australian general practitioners were against the generic medicines because of lacking confidence on its efficacy and safety, some others supported the generic prescribing as because of cost advantageous to patients but the majority didn't know any of the bioequivalence and bioavailability studies by the FDA [61].

According to a survey in Malaysia involved general practitioner, only [4.6%] of the respondents were aware of the bioequivalent standard protocol of generic products, however about half of the respondents were either agreed or strongly agreed with the bioequivalence between generic and brand-name drugs [62]. About [33 %] of the respondents were not confident about the efficacy of generic and [10.3%] thought that it may cause higher side effects than the brand. Although [45%] of the general practitioners admitted the role of drug companies advertisement in the prescribing patterns, the majority pointed out other factors as information about the efficacy and safety of generic medicines, patient affordability and the manufacturer/supplier credibility and reputation. Tsiantou *et al.* recorded the factors affecting the physician' prescribing decision and their perception towards generic prescribing, the respondents reported that their information sources were publications [72.8%] peer-reviewed journals, [69.6%] conferences and [60.5%] medical textbooks, medical sales representatives and electronic database [63]. However, they have reported that physicians prescription decision didn't affect by medical representatives although it was considered the second main source of information. Despite the positive perception towards the efficacy and safety of generic drugs, [19.5%] of respondents

reported that they chose generic medicines due to their lower cost.

2- Pharmacists' perspectives on generic substitution

The pharmacists have a key role in the healthcare system, besides being the source of drug and drug interaction information to physicians, supply patients with drug information, recommend the over-the-counter medications, they assist in reducing prescription spending by recommending generic substitution [36, 64]. Olsson and Sporrang revealed that pharmacists found that generic substitution decreases the costs for drugs but also they pointed out that generic substitution can bother patients, which could result in less benefit from treatment [64]. Generic substitution is a common practice with pharmacists, but the laws governing generic substitutions vary from mandating pharmacists to substitute brand drugs with therapeutic equivalent generics to allowing pharmacists to perform generic substitution and requiring patients' consent [65]. Indeed, pharmacists are in a unique position to recommend generic medicines and help patients with cost-saving of generic substitution. In a study by Mott and Cline examining the rate of generic drug prescribing and the rate of generic substitution by pharmacists, they have shown that pharmacists generically substituted [83.8%] of prescriptions that could be generically substituted [66].

Substitution of brand-name drugs with generic drugs could reduce the costs for medicines, however, switching to generic medications in most cases seeking patient affordability [67]. Allenet *et al.* reported that [91%] of the community pharmacists' respondents in France were satisfied to have substitution rights as it enhances the role of the pharmacist as drug expert in the healthcare system. [43%] relay on systemically offering patients generic medications [68]. Chong *et al.* have reported that pharmacists recommend generic substitution in the Australian community regularly that occupied [96%] of the whole purchases. Patient acceptance for generic substitution was higher in remote areas than in urban although the recommendation is higher in urban than remote areas [69]. Toklu *et al.* evaluated the community pharmacist perception towards generic drugs and indicated that there was no difference between the generic and brand-name drugs, however [40%] had a concern regarding the bioequivalence of the generic drugs [70]. Besides, half of the pharmacist indicated that they substituted generic by themselves. Carroll *et al.* reported many reasons influencing the pharmacist behaviour on generic substitution, the risk of non-therapeutically equivalence, non-bioequivalent products and concerns regarding product quality [71]. In Egypt, while there is a strict measures where the physician is the only prescriber, but the pharmacist has an influential role in either switching or even prescribing medications for patients who came with only symptoms.

3- Patients' perspectives on generic substitution

Patients' perception is an important factor influencing generic drugs initiation. Therefore, providing the patient with sufficient information about generic medication that may reduce the cost with equitable care is crucial [72]. Many patients determined their approval to generic initiation or substitution if recommended by their physician or pharmacist as they feel comfort towards the efficacy of the drug in addition to the cost consideration that influences patients' decision to utilize generic medications [73].

There were a mixed views of patients towards the knowledge of generic drugs and their quality and effectiveness. Sharif *et al.* have demonstrated in a survey in the United Arab Emirates that patients had a poor knowledge of generic and brand medicines; and they concluded that the patients' poor ability to differentiate between generic and brand drugs could be improved if both pharmacists and physicians communicated more with their patients and educated them about the correct selection between generic and brand drugs [74]. According to the European generic medicine association survey in 2004 revealed that patient co-payment in the form of a percentage of the cost, difference above reference price or a fixed amount per prescription make the patient more economically responsible over their medication and demand cheaper medications [41]. Al-Gedadi *et al.* in a survey on the consumer perception towards generic medicines have reported that [28.3%] knew the meaning of generic medicines and [33.9%] of them got their information from pharmacists, [25.9%] from physicians and the rest from newspaper and mass media [75]. Additionally, regarding the consumer's perception of the generic drugs quality, [39.8%] reported that generic drugs had lower quality than brand drugs. Stewart *et al.* reported that 228 [51.6%] out of 441 of participants heard about generic medicines and about [78%] of the participants expressed their agreement towards switching into generic medicines in cases of mild illness like cold, flu and fever, however [58.7%] in case of series conditions upon pharmacist recommendations [76]. Many reasons were documented for not wanting to substitute generic with brand-name because of their physicians and pharmacists, some of consumers believed that generic drugs could cause side effects higher than branded drugs, some consumers stated that there was no significant difference with the price of both of them, some consumers complained about the appearance of generic [colour, packaging..etc] and others they were worried about their efficacy compared to the originator [76].

Kjoenniksen *et al.* have revealed that [24%] of the respondents got their knowledge about generic drugs from a physician, while [53%] from pharmacists. Patients with polypharmacy were 2.6 times higher in generic substitution than other consumers. About [36%] of patients who switched to generic medicines has a negative perspective towards the generic drugs and [18%] were dissatisfied with the efficacy of generic compared to the branded medicine [77]. According to Heikkilä *et al.* survey on Finn's generic substitution, [34%] of respondents had substituted medicine at least once and [66%] of them substituted their medicines to save money or upon the pharmacy recommendations [78]. Likewise, Australian's consumers perception towards generic drugs, all respondents knew the term generic medicines and were aware of the availability of generic drugs but they commonly used the term cheaper instead of generic drugs [79]. Moreover, the Australian's consumers reported several reasons for not accepting generic drugs including branded drugs prescribed by the general practitioner, trusting branded medicines, concerns regarding the safety and efficacy of generic medicines owing to poor information.

4- Economic and commercial perspectives

The pharmaceutical cost is considered the second-highest cost in the healthcare system after staff cost. Different reasons contribute to increasing pharmaceutical expenditure including the rise in population risk factors, intensifying in disease prevalence, changes in clinical threshold in treatment and development of new medications [80, 81]. In the United States,

spending on drug prescription is the highest all over the world. From 1980 to 2000, it increased from 12 to 121.8 billion dollars, however, it exceeded 250 billion dollars in 2005. The net spending raised approximately 20% between 2013 and 2015 and constituted 17% of the total healthcare [72, 82, 83]. In Canada, spending on drugs increased from 9.5% in 1985 to over 16% in 2004 of the total health where its annual growth rate outpace all health expenditure in that period [84]. Medicine spending accounts for 20-60% of the total healthcare spending in low-middle income countries [47]. The total healthcare spending in Egypt is 61.4 billion LE [Egyptian pounds] in the period from 2008 to 2009 and 34% of the total cost was spent on medications [85]. As the public health insurance in Egypt covers only 58% of the population and public health hospitals adapt to a list of drugs so patients pay out of pockets to get their medicines [47]. The annual amount of pharmaceutical industry in Egypt has reached 15 billion LE in 2009, which is approximately equivalent to 2.7 Billion dollars. Besides, the local industry covers around 82% of the market needs with affordable medicines, while the remained medicines [18%] are imported pharmaceuticals [49].

In France, the estimated annual cost savings reached 1 billion Euros in 2007, 0.905 billion Euros in 2008 and 0.1 billion Euros in 2009 results from the prescribing and dispensing generic medicines [86]. In Portugal, the estimated potential savings from generic substitution were around 110 million Euros however the size of savings varies widely according to the active constituent used as it ranged from 3.5 million Euros for Ramipril to 40 million Euros for Ethinylestradiol. These obvious savings results from the policy and regulation of the government there that aid in reducing the expenditure on originating medicines by 45% [36].

In 2010, the cost savings in American healthcare system reached 1.07 trillion dollars between 2002 to 2011 with an average 158 and 192.8 billion dollars in 2010 and 2011 respectively these results from the increase in generic drugs use also according to the analysis of Generic Pharmaceutical Association revealed that the US economy saved 931 billion dollars between 2001 to 2010 owing to prescribing generic medicines [25, 87]. According to the Greater Manchester Medicines Management Group [GMMMG] generic prescribing guidelines, increasing generic prescribing from 20% to 84% respectively from 1976 to 2013 had led to save around 1.7 billion Euros for the national health system and conserve 490 million items for prescribing without extra spending [88].

Drug shortage is a problem worldwide that faces many healthcare systems [89-91]. Higher percentage of physicians reported drug shortage-related deaths due to inadequacy of drug availability and accessibility of medications [92, 93]. Healthcare professionals' behaviors may contribute to detrimental outcomes of drug shortage, patient's anguish of getting drug treatment, increased suffering, deterioration of patient condition and finally death [94]. In Egypt, current pharmacy practice law prohibits substituting prescription medications without permission from prescribers [95]. Egyptian Pharmacists Syndicate demanded to adopt International Non-proprietary Name prescribing policies to facilitate dispensing analogous products especially during drug shortage. In the light of Egypt's limited healthcare spending and most spending on medicines is out of pocket, generic prescribing must be made as a common prescribing practice as brand name drug costs continue to be a burden for many patients [96]. Therefore, generic prescribing represents a major opportunity to overcome limited resources, drug affordability and costly treatment. It is becoming a

demanding issue for policy makers in Egypt to develop a generic policy to achieve better effectiveness and economic utilization from medicines prescribing. Interprofessional collaboration between physicians and pharmacists would curb drug shortages and resolve profession conflicts.

Physician-pharmacist collaborative practice

The pharmacist influencing role in prescribing medicines is an important part of the physician-pharmacist working collaboration [97]. McDonough *et al.* had established a model for a pharmacist-physician collaborative working relationship that included multiple stages during prescribing process [98]. Stage zero for professional awareness that included the enrolment of the pharmacist in dispensing medications and detection of adverse effects and any interactions that might happen to inform the physician besides answering drug information requests. Stage 1 for professional recognition in which the pharmacist work on providing the physicians with the resources to help in their practices also pharmacists in this stage promote their help through supplying physicians with patient medication history and adherence information. Stage 2 for exploration and trial, the physician referred the patients to the pharmacy to ensure the pharmacist's skills and competence through the quality of care given to the patients. Stage 3 and Stage 4 expansion and commitment of the professional relationship in which collaboration occurs, communication became bilateral and interdependence became deep.

Physician and pharmacist work on an effective and safe prescribing which can be reached by knowing the dose, regimen, pharmacology, side effects, adverse effects, drug-drug interaction, drug-diet interaction, drug-disease interaction and drug monitoring. Dependant prescribing allows the pharmacist to engage in the prescribing process through prescribing protocol, formulary, patient referral and collaborative prescribing these results in effective physician-pharmacist collaboration [97]. Kucukarslan *et al.* stated that the collaboration between physicians and community pharmacists improve patients adherence to their medications and increase the use of cost-effective medications in addition to decreasing the incidence of drugs therapeutics problems [99]. It has been reported that the enrolment of the pharmacist with general practitioners in prescribing medicines increases the generic prescribing rate as well as financial incentives with educational intervention and audit/feedback could be effective in supporting of generic prescribing [45]. It is becoming important that physicians and pharmacists should cooperate to manage drug shortage and find the appropriate substitutes and alternative products to achieve the best therapeutic outcomes [100].

Conclusions

Generic medicines are very important in treating and preventing various conditions worldwide through enhancing the affordability and accessibility of drugs among patients. Physicians have mixed views regarding the quality, efficacy and safety of generic medicines, despite their good perception regarding the cost savings of the generic medicines, most of them have concerns about the safety and efficacy due to the lack of clinical trials and the difference in the regulatory systems and policies of the generic drug approval. Additionally, the majority of physicians didn't know the generic counterpart of the brand-name drugs because of the lower number of pharmaceutical

sales representative visits of generic companies compared to brand-name companies.

Most of patients were willing to use generic medicines if it is recommended by their physicians and pharmacists because of the cost savings. Much evidence-based information regarding the bioequivalence, efficacy and safety between brand-name and generic medicines is needed to convince physicians, pharmacists and patients about the quality, effectiveness and economic utilization of generic medicines. Educational and promotional efforts for generic medicines should also be improved. Strict policies that control medicines prescribing and generic substitution are needed in Egypt to enhance the use of generic medicines. Interprofessional communication and collaborative practice among healthcare professionals can attain better therapeutic outcomes and achieve positive patient outcomes. This collaboratin can also help to curb drug shortages and reduce the economic burden of drug treatment by finding the appropriate analogues and alternative drug products.

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