Polypharmacy, artificial intelligence (AI) and rational medication prescribing – The new frontier

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Key words
Polypharmacy, Artificial intelligence, Drug interactions, drug-drug interaction, Medication interactions, Adverse events, Elderly, Pharmacovigilance, Medications, Medication prescribing, Risks, Ethics, Safety

Executive Summary

Clinical rationale (Importance)

- Healthcare practitioners, including dentists, have an obligation to be vigilant of the risks and adverse effects associated with medication-medication (MMI's) and medication-disease interactions (MDI's), when prescribing medicines, especially in the elderly and at-risk groups taking multiple medicines, to avoid harm and minimize adverse effects, and to promote safety and quality of health care.
- Artificial intelligence driven Clinical Decision Support Systems (CDSS's) could potentially optimise polypharmacy and reduce medication-related harm in older adults.
- This review summarizes the current understanding of polypharmacy and the application of AI in rational medication prescribing.

Key points

- Polypharmacy is complex, uncertain, and a challenge for clinicians due to the vast number of factors that influence drug use and response.
- The risk of medication toxicity and harm due to MMI's and MDI's is generally higher in older people with multimorbidity, frailty and those taking at risk medications.
- Distinguishing between appropriate and inappropriate polypharmacy is an complex, and challenging issue for a clinician.
- Artificial Intelligence (AI) could be an important auxiliary tool to enhance complex clinical decision-making when prescribing medications.
- AI driven CDSS's to facilitate rational medication use is still in development stage.

Practical applications

Dentists need to adhere to the following principles to minimize inappropriate polypharmacy prescribing, medication interactions and adverse events:

- Regularly review patient medical history and records.
- Stay updated on clinical pharmacologic knowledge.
- Communicate treatment needs and medications to other health care providers.
- Consult with the patients' health care practitioner(s) when prescribing to high-risk patients.

Background

Polypharmacy, or the use of multiple medications for treatment of multiple chronic diseases in the elderly population, is on the increase globally[1-5] and is a leading cause of unexpected adverse effects (or events) (AEs), compromising the safety and quality of health care.[1,6] Unwanted medication-medication interactions (MMI's) and medication-disease interactions (MDI's) due to polypharmacy that might cause unexpected adverse events (AE's), remain a significant and challenging issue to health care practitioners.[7] Risk management strategies and pharmacovigilance are also crucial when a high-risk medicines are prescribed to patients who are particularly vulnerable to adverse effects.[4]

Abovementioned trend is compounded due to prolonged life expectancy and rapid acceleration of populations aged 65 and older,[8-10] the co-existence of multiple chronic diseases, age-related changes in pharmacokinetics (PK) and pharmacodynamics (PD),[11-17] fragmented health care services (i.e., dental, medical, specialist, hospital, and self-medication prescribing), and use of supplements and herbal medications. Fragmented health services has resulted in lack of co-ordination of prescribed medicines. Furthermore, patients unintentionally do not tell their health care providers what medications, supplements,

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nutrients and drinks they are taking, unless specifically asked.[5] According to the World Health Organization, adverse reactions caused by prescribed medicines are among the top ten leading causes of death in many countries.[6] The impact of use of various combinations of multiple medications on individuals' health and burden on the health care system is largely unknown,[18] and effective tools to address these challenges remain elusive.[19]

Potential MMI's and MMD's in elderly patients, with multi-morbidities, and those taking high-risk medications, makes it extremely difficult and challenging for clinicians to make treatment and rational prescribing decisions to maximize benefit and minimize harm in polypharmacy cases.[20] Therefore, predicting medication interactions and adverse events accurately can significantly improve clinicians' ability to make better decisions and establish optimal and safe treatment regimens. However, manually detecting these interactions is complex, time-consuming, labour intensive and challenging for clinical decision-making.[21]

In the health care field, the use of artificial intelligence (AI) as an auxiliary decision-making tool is a new and developing field aimed at enhancing the clinicians' ability to accurately predict and avoid untoward MMI's, MDI's and adverse events [7,11,20-27] and to facilitate pharmacovigilance and rational medication use.[22,28]

The aim of this narrative review is to contribute to a deeper understanding of the current scientific evidence relating to polypharmacy and its associated risks and consequences, surveillance, as well as the role and use of AI to facilitate rational medication use and to minimizing potentially harmful adverse events due to MMI's and MDI's.

Polypharmacy

• *Clinical significance*

With aging, the risk of developing multiple chronic diseases increases. Subsequently, the number of medicines prescribed or used, potentially inappropriate prescribing and potential MMI's, MDI's and AE's resulting in potential harm to the patient, also increases.[11,29-34] Polypharmacy, has become a safety and quality issue and a public health concern due to the increasing risk of MMI's and MDI's resulting in potential serious adverse reactions and harm to patients.[11,12] It is reported that the risk of developing side effects was 15% with the use of two medicines, 58% with the use of five medicines, and increased to 82% with the use of seven or more medicines.[35,36]

• *Definition and nature*

Polypharmacy is defined as the simultaneous use of multiple medications by the same individual for simultaneous treatment of multiple conditions.[11,37]

It is common medical practise for patients to be safely prescribed more than one drug, thus benefiting from the simultaneous treatment of multiple conditions. This practice, especially where it involves more than five medications (≥5), is called polypharmacy,[38-,41] whereas with extreme polypharmacy referring to ten or more (≥10) medications.[42]

The concept of polypharmacy is often studied as a static exposure to medications without considering past medication use or subsequent changes, age, presence of co-morbidities, use of supplements and herbal medications, dietary and alcohol intake, which may limit the conclusions about the consequences of polypharmacy.[18] Patients often look for treatment of the associated new symptoms, but any potential link between the symptoms and the medicines they are already taking may go unrecognised by the healthcare professional. Patients may therefore be prescribed new medicines to counter the adverse effects of the prescribed medications, thus inadvertently worsening the problem.[43]

Polypharmacy, represents a potential for harmful health consequences for the patient due to:
(i) interaction between medications because of pharmacological interactions or pharmaceutical incompatibility; (ii) prescribing medicines in the presence of contraindications and restrictions to use, irrespective of taking into account the main and concomitant diseases; (iii) prescribing medications without regard to age restrictions; (iv) unwarranted co-administration of excessive quantities of medicines for the treatment of the same disease; or (v) exceeding the maximum permitted daily dose, without taking into account the method of the drug application and body weight.[6,20,44,45]

Although there are circumstances in which the prescription of multiple medications is appropriate and leads to improved health outcomes, distinguishing between appropriate and inappropriate polypharmacy is a complex and challenging issue for the clinician.[46]

Appropriate polypharmacy is present when: (a) all drugs are prescribed for the purpose of achieving specific therapeutic objectives that have been agreed upon with the patient; (b) therapeutic objectives are actually being achieved, or there is a reasonable chance they will be achieved in the future; (c) drug therapy has been optimized to minimize the risk of adverse reactions; and (d) the patient is motivated and able to take all medications as intended.

On the other hand, polypharmacy becomes inappropriate when the risks of multiple medications begin to outweigh their potential benefits for an individual patient.[4] Inappropriate polypharmacy is present when one or more drugs are prescribed that are not or no longer needed, either because (a) there is no evidence-based indication, the indication has expired, or the dose is unnecessarily high; (b) one or more medicines fail to achieve the therapeutic objectives they are intended to achieve; (c) one drug or the combination of several medications causes inacceptable adverse reactions or puts the patient at an unacceptably high risk; or because (d) the patient is not willing or able to take one or more medicines as intended.[4]

• *Prevalence of polypharmacy*

Polypharmacy is the rule rather than the exception among elderly people living with chronic diseases and pain.[47] There is some evidence of rising rates of polypharmacy, including

prescription medications, over-the-counter medications and dietary supplements, and potentially serious MMI's, resulting in adverse medication events in both outpatient and inpatient settings.[2,3,14,48,49,50]

The prevalence of polypharmacy ranges from 34% to 65% in elderly patients.[31,51,52] The pooled estimated prevalence of polypharmacy in the 54 studies reporting on polypharmacy in all medication classes was 37% (95% CI: 31-43%)[53] Participants reported using an average of 6 medications (median: 5) the prevalence of polypharmacy was 71.4% (95% CI: 69.0–73.8) and excessive polypharmacy (≥10 medications) was 25.9% (95% CI: 23.6–28.3).[47] Receipt of ≥10 medications was strongly associated with increasing age ≥80 years (24%), but was also independently more common in people living in more deprived areas, and in people resident in a care home.[54]

• *Risk factors associated with polypharmacy*

The risk of polypharmacy-related side-effects or adverse reactions due to MMI's (including over the counter medications, supplements, and nutrients) and MDI's are higher in the patient populations with co-morbidities, advanced age, and frailty, and thus a key challenge to clinicians.[1,4,11-13]

The most frequent patient-related risk factors associated with polypharmacy include: (i) multiple chronic medical conditions, (ii) patients aged 75 and older, (iii) frequent hospitalization and emergency room visits, (iv) frailty, cognitive impairment, nursing home placement and residency in a long-term care facility, (v) self-treatment by use of over the counter medications or herbal supplements, (vi) overuse, underuse and misuse of medications, and (vii) socioeconomic factors such as lack of access to consistent care and inability to afford medications.[11,20,28,55,56,79] The number of medications prescribed was the characteristic most strongly associated with serious side effects (10.9% if prescribed 2–4 medications vs. 80.8% if prescribed ≥15 medications).[54]

The physiological changes that occur in ageing can affect PK and PD, which in turn can impose considerable variability in medication management for older adults with polypharmacy. Age-related changes in PK/PD include changes in drug absorption from the gastrointestinal tract, plasma protein binding, drug distribution, reduced hepatic metabolism and clearance, altered renal function, changes to receptors and voltage-gated channels, and changes to the autonomic nervous system.[57]

Other health system related risk factors associated with polypharmacy include: (i) segregation of medical and dental care, (ii) lack of provider-provider care coordination, (iii) use of multiple physicians from different specialities, (iv) keeping poor medical records, (v) insufficient knowledge of the heath practitioner about medicine interactions and side effects, (vi) limited clinician time to review and assess adverse reaction profiles of multiple drugs, and (vii) limitations in medication information resources to evaluate multiple MMI's.[11,58-61] In many studies in the literature, it was shown that the biggest obstacle to rational medication use in the case of polypharmacy is "time constraint".[11,62,63]

• *Consequences of polypharmacy*

Although it is common medical practise for patients to be safely prescribed more than one medication, it has been shown that an intake of at least five medications significantly increases the risk of adverse events.[64,65] Increasing medication interactions due to polypharmacy can give rise to adverse reactions where the effect of one medication is changed in the presence of other health professional- or self-prescribed medications or supplements, potentially resulting in increased toxicity and potential harm to the patient.[36,66-68] The PD effects of medication interactions can have a synergistic, antagonistic, or additive effect, and the PK effect of interactions are due to decrease or increase of absorption, distribution, and excretion factors influencing medication metabolism.[69] Approximately 10% of consultations in a primary healthcare setting are related to adverse medication reactions and 60–70% of serious adverse events are preventable but are often inadvertently overlooked.[70,71]

There is mounting evidence that frequent occurrences of adverse effects resulting from polypharmacy-related medication interactions has been associated with a plethora of harmful health consequences, such as frailty, falls, cognitive decline, delirium, incontinence,[72-75] increased morbidity, treatment costs, hospitalization, and in some circumstances, death.[19,31,51,52,72-74,76-82] Polypharmacy thus represents a potential public health threat, a major source of greater use of health care services and a financial burden for the health care system.[9,44,45,83-86]

Close monitoring and evaluation of the different medications used are therefore important, especially in elderly people and those with limited access to care.[47] Considering the multiple variables that may impact on medication interactions and adverse effects, mitigating the consequences of polypharmacy and promoting rational medication use in real time can only be done with the use of AI.[6]

Role of artificial intelligence (AI) in polypharmacy related clinical decision support systems (CDSS's)

• *What is artificial intelligence?*

AI can broadly be defined as computer systems powered by mathematical algorithm-based predictive models to process and analyse huge amounts of robust datasets (also referred to as 'big data analytics') in a way that resembles intelligent human behaviour, to perform cognitive tasks such as visual perception, speech recognition, decision-making, and translating between languages.[87-90]

It encompasses a wide variety of technologies including: machine learning (ML), deep learning (DL), natural language processing (NLP) and neural network (NN) algorithms and computational models that can analyse, recognise, reason, interpret, predict, plan, learn, interact, and respond to text, images or languages.[7,91]

AI automates repetitive and progressive learning and discovery through exposure to new data and adjusts to new inputs as it goes along and incorporates real-word clinical

experiences, and new scientific data to produce predictions and/or recommendations.[7,88,91] However, the collection, use, and communication of personal health information to train AI algorithms raise unique legal and ethical concerns and require a responsible approach.[92]

AI has become more popular today due to increased data volumes, advanced algorithms, and improvements in computing power and storage.[91] The goal of AI tools is "to provide software that can reason on input and explain on output."[91] "AI will provide human-like interactions with software and offer decision support for specific tasks, but it's not a replacement for humans – and won't be anytime soon."[91]

Big data analysis techniques as a part of eHealth, and foundation of AI, were introduced in 1997, [93] with the purpose of analysing increasing volumes of raw data and a variety of complex databases, faster and more accurate in real time to improve clinical decision-making.[94-96] Studies have showed that the biggest obstacle to rational medication prescription in practice is "time constraints. It is suggested that an AI web application as an auxiliary tool could analyse age, medications, and diseases specifically for the patient 60 times faster than the manual method, and provide quick access to the relevant references, and ultimately supports rational medication use, and eliminate prescription of potentially inappropriate medicines to the patient.[11]

Advances in computing power, growth and availability of large-scale patient databases, and machine learning algorithms, have now provided the capacity and capability to integrate various data sources and analyse complex inter-relationships between risk factors and outcomes at the point of care.[90] AI-powered clinical decision support systems (CDSS's) can potentially assist health professionals in making informed decisions regarding polypharmacy.[28]

• *Clinical significance of AI*

According to the SAS Institute "unleashing and role and the full potential of data to enhance knowledge and clinical decision-making in the health care domain is now becoming more important than ever."[91] Ensuring that medicines are prescribed safely is fundamental to the role of healthcare professionals who need to be vigilant about the risks associated with medicines and their interactions with other medicines (polypharmacy). One aspect of preventative healthcare is to use AI to identify patients at risk, to inform clinical decision making in real time, to facilitate optimisation of medication prescriptions, prevention of MMI's and MDI's, to reduce the frequency, duration, and severity of AE's, and to promote safety and improve quality of care.[28,90,97-101]

Determining medication interactions and health outcomes associated with polypharmacy requires considering concurrent and sequential analysis of multiple medications, PD's, PK's, duration of treatment, medical and sociodemographic characteristics of individuals. This type of analysis of large amounts of complex heterogenous data, can only be accomplished with AI powered CDSS's to generate predictions or insights into MMI's, MDI's and potential adverse reactions, to solve health care challenges and to inform and support clinical decision-making relating to appropriate medication therapies, dosages, and combination medications (polypharmacy) in at risk populations such as the elderly.[7,18,20,91,102] Thus the goal of electronic CDSS's (AI) is to assist primary health care practitioners to make informed clinical decisions to optimise safe prescribing of medications in polypharmacy and reduce medication-related adverse events and harm in older adults.[11,20]

• *Current status of AI CDSS's*

AI has positioned itself as a supportive technology in many domains, including the health care industry.[103-107] AI driven big data analysis techniques and algorithms currently exist in other contexts, but they are rarely used in healthcare.[101] Rapid technological advancements in AI, robotics, cloud computing, and The Internet of Things, are transforming the health care industry and challenging ideas about how health care providers should diagnose, treat, prescribe, and manage everyday health care problems.[87,107]

Recently, various studies have been undertaken to investigate the use of AI for analysing health record data to facilitate the surveillance, decision-making and prevention of polypharmacy.[6,18,108,109] Furthermore, many exploratory and review articles have discussed the current status and limitations of AI systems in the management of polypharmacy. [7,11,21,33,110-115]

It is not yet known if AI tools are potentially useful in the identification of patients with polypharmacy and thus the reduction of the risk of adverse events caused by multiple medications.[101] However, the development of CDSS's has been identified as a key facilitator in uptake of AI's tools in busy clinical practice, and a step towards precision medicine in polypharmacy.[20]

Mouazer and co-workers have provided a global overview of different electronic CDSS's that currently exists for the management of polypharmacy in the elderly population.[112] Most of the systems are devoted to pharmacists without a link to electronic health records. Furthermore, none of the systems used machine learning algorithms, and only a few systems were evaluated in terms of effectiveness, efficiency, and user satisfaction.[112]

With this first and only artificial intelligence-supported web application, which is prepared with the 430 most used pharmaceutical agents in the market and outputs simultaneously in three categories, it is aimed to facilitate the detection of patient-centered interactions, provide quick access to the relevant bibliography, and ultimately to support the rational drug use for the clinicians.[11] The proposed web application is publicly available at (https://fastrational.com/.)

• *Limitations of AI use in polypharmacy*

Conventional AI-based systems still have several drawbacks.[7] Real-world patients are complex, each characterized by individual clinical, medication, demographic, genetic, microbiome, and lifestyle factors. Current AI tools lack intelligent algorithms to

account for these multiple factors and their potential complex medication interactions.[20] Current medication-medication prediction models only consider effects for two medications. There is little knowledge available of interaction effects between 3> medications.[20] Furthermore, most of the known polypharmacy effects are highly variable and non-specific and usually not detectable in clinical trials.[116]

Multiple data sources are required improve machine learning to achieve better prediction accuracy. Information on the presence and severity of MMI's often vary according to databases.[117] The surge in the predictive performance of AI tools is achieved by increasing model complexity. This turns these models into black-box systems and causes uncertainty regarding their operation mechanism. This ambiguity and bias hinders the wide adaptation of AI models in critical domains like healthcare.[7] ML-based models are learned from positive and negative data, making it difficult in real-world domains due to the lack of true negative MMIs or a ''gold standard" non-MMI. Currently it is difficult to identify positive data from many un-labelled data containing positive and negative data samples to avoid biased sampling and ambiguity.[7] Currently, the generative systems that power AI tools are prone to "hallucinating false content" and "false responses" because they are limited to access to abstracts of scientific papers incomplete medication and patient databases. Without complete and comprehensive scientific, biological and clinical databases and full-text scientific literature availability the quality of AI responses may be biased, inaccurate and questionable.

AI-CDSS's in geriatrics can be a great asset, especially when dealing with patients with cognitive disorders. By using AI-CDSS's, older patients' values and beliefs might be overlooked, and the quality of the doctor-patient relationship might be altered, endangering compliance to the 4 fundamental ethical principles of non-maleficence (do no harm), beneficence (do good), autonomy (respecting the patients right to make informed decisions) and justice (fairness).[115]

Some of the most common disadvantages of using AI include, bias and discrimination, privacy and security concerns, lack of transparency and accountability, dependence on technology and absence of human contact.[88,118]

It is important that these potential limitations be considered in the development and implementation of AI systems in the health care field and that regulation and controls are in place to mitigate potential adverse effects. It is also important to ensure that AI systems are used as tools to assist physicians and other health care professionals, rather than replacing them.

- ***Medication Interaction Checkers***

Currently, there are some freely available desk-top web applications for MMI's (drug-drug interactions) detection such as:
Drugs.com: Solid offering that is made nearly unusable by ads interspersed with interactions. https://www.drugs.com/drug_interactions.html
Epocrates Interaction Checker: Unfortunately behind a free registration wall. Registration required. https://www.epocrates.com/online/interaction-check
Medscape Interaction Checker: Easy-to-use and well designed. Interactions are updated instantly upon each edit to a drug regimen. https://reference.medscape.com/drug-interactionchecker
WebMD: Minimalist and easy to use drug interaction checker from WebMD. https://www.webmd.com/interaction-checker/default.htm
Drugbank Online: Limited to 5 drugs and includes limited results. https://go.drugbank.com/drug-interaction-checker

The abovementioned web-applications only provide information about the interaction of medicines with each other (MMI's) rather than evaluating the patient holistically along with age, food, and drinks (medication- food interaction) and diseases (MDI's).[11] Although they are important tools for rational medication prescribing, they provide more standard information rather than a patient-centered approach because they ignore the existing diseases, medications, or age of the patient.

Other medication interaction checkers offered on purchase (subscription-based) include:
Stockley's Interactions Checker:
https://www.pharmaceuticalpress.com/products/stockleys-interactions-checker/
PEPID: Comprehensive medication database and simplified all-tool functionality App to highlight the features and selections users want most. https://pepid.com
Micromedex: Enhanced for advanced searching online or App, ability to compare medication results, and aggregation with other information resources.
https://www.micromedexsolutions.com/home/dispatch/
Lexicomp: Available online and mobile. Delivers automatic content updates, both saving time and ensuring the clinicians are using the latest evidence-based content when treating patients.
https://go.wolterskluwer.com/rs/591-WJW-115/images/Lexicomp%20Business%20Review.PDF
DynaMedex: Solution designed to combine medication and disease content into a single-source for evidence-based insights. https://www.dynamedex.com

Most desktop web-application medication-medication checkers (drug-drug) categorise interactions as follows:
(i) Contra-indicated (never use this combination of medications because of high risk of dangerous adverse events); (ii) Serious (potential for serious interaction that requires regular monitoring by the prescribing doctor or physician, alternative medication may be required; (iii) Significant (potential significant interaction-monitoring by the prescribing doctor/dentists is likely required; and (iv) Minor (interaction is unlikely, minor, or insignificant).

Ensuring that medicines are prescribed safely is fundamental to the role of healthcare professionals who need to be vigilant about the risks associated with MMI's.[28] Although AI can assist the medical and dental fields in many ways, still, the final decision must be made by the professional as the overall treatment is a multidisciplinary approach.[119]

Polypharmacy and practical guidelines for the dental practice setting

• Patients with the highest risk of inappropriate polypharmacy are those with the age above 65, older people, presence of multimorbidity, greatest frailty, on >5 medicines, and taking high-risk medicines.[120] Optimizing medication prescribing in at risk patients is complex and includes: deciding what medication is indicated, choosing the best medicine, determining a dose and schedule appropriate for the patient's physiologic status, monitoring for effectiveness and toxicity, educating the patient about expected side effects, and indications for seeking consultation with the patients general practitioner, physician or pharmacist. [78]

• While elderly patients, co-morbidity and polypharmacy encounters in the dental practice are a reality and AI driven CDSS's are still in early development stage and therefore unavailable,[20] dentists' first point of reference to ensure safe prescribing and prevention of polypharmacy related adverse reactions and complications, is consultation with the patients' GP, physician, or pharmacist. Dentists are also advised to use a medication checker or MIMS reference in the absence of a primary health care provider or specialist for advice.

• Regularly review every patients' chronic medication, whether, prescribed, OTC, supplemental, herbal, or traditional remedies. Many medications need to be used with special caution because of age-related changes in PK (i.e., absorption, distribution, metabolism, and excretion) and PD (the physiologic effects of the drug).[78]

• AE's can be prevented by having a good knowledge of prescribed medications, their associated risks and interactions with other medicines, being vigilant and monitoring their patients, and by being prudent in their prescribing habits.[121]

• Ensure that patients are engaged in decisions made about their medicines and are empowered and supported to do so.[4] Communicate frequently with the patient and check medical records regularly.

• Regularly review the patients' medical history for co-morbidities, conditions and medications that could affect renal and hepatic function bi-directionally, before making decisions about the appropriateness of medications.[4] Age-related changes in medication clearance due to renal or hepatic impairment or MMI's could potentially result in adverse events. Therefore, it is important to review the dose of medication in patients with impaired organ function, "using a start low, go slow approach, with careful titration while monitoring effects and adjusting drug doses in a timely fashion."[4]

• Some medications, including non-steroidal anti-inflammatories, corticosteroids, anti-coagulatants,[122] antipsychotics, antidepressants,[123] benzodiazepines, centrally acting analgesics,[124] anticholinergics,[125,126] and antihyperglycemics,[127] are classified as high-risk for inappropriate prescribing and frequently implicated in medication-related hospital admissions.[128-130] Dentists should be prudent when prescribing to patients using risk medicines. When in doubt consult with the patients GP or physician first before prescribing.

• Check for interactions between medications, herbals, vitamins, and alcohol. Listed tools are free to use and with few exceptions do not require registration. Always consult with the patients' medical practitioner, specialist or pharmacist about possible interactions before starting a new medication.[20]

• Educate patients to keep all their prescriptions at one pharmacy.[131]

Conclusions

Polypharmacy is highly prevalent in elderly patients with multi-morbidities, and frailty and are more likely to experience AE's. Polypharmacy-related MMI's and MDI's has been associated with a plethora of harmful health consequences, represents a potential public health threat, a major source of greater use of health care services, and a financial burden for the health care system. Polypharmacy can be appropriate but is problematic or inappropriate when the increased risk of harm from MMI's, or MDI's, or the burden of administering and monitoring medicines, outweighs plausible benefits.

Dentists have an obligation to prescribe medicines safely, to be vigilant about associated risks and interactions when prescribing medicines, to avoid harm and minimize adverse effects resulting from prescribing medications. Rational use of medication prescribing in polypharmacy is particularly challenging because of the vast number of interacting factors that can influence medication use and response.

AI has increasingly become an integral part of health care that is set to have an undeniable impact on clinical decision-making, and the improvement of safety and quality of health care. While the potential benefits of AI driven CDSS's to optimise polypharmacy and to reduce medication-related harm in older adults are widely recognized, its implementation in facilitating rational prescribing of medications is still in its early stages of development and not yet available to health care practitioners. In addition, it has become increasingly difficult for health care practitioners to coordinate, integrate, monitor, and evaluate all patient-, health system-, genomic-, medication-related variables and associated risk factors. This process requires awareness, knowledge, special skills and time. Although the unleashing and role of the full potential comprehensive data bases to enhance AI knowledge and clinical decision-making in the health care domain is now becoming more important than ever, trusting machines to make these decisions for a clinician, remain a challenge in the AI domain because of lack of appropriate big data, transparency ethical and legal issues, and the issue on removal of bias.

The role of dentists in prescribing medications is not much discussed in the scientific literature, although the proportion of elderly patients with co-morbidities requiring comprehensive dental care has gained momentum. This comes with the associated polypharmacy burden, requiring pharmacovigilance before and after any routine prescription is made. Various 'MMI checkers' are freely available and dentists are encouraged to use these web applications for

the benefit of the patient. However, these application are currently limited in their effectiveness as they do not take age, co-morbidities, foods, drinks, and over the counter supplements into consideration.

Prudent use of medication prescribing is critical to provide safe and quality health care. This requires knowledge of deciding what medication is indicated, choosing the best medication, proper use of selected medicines, avoiding inappropriate medicine prescribing, monitoring adverse medication effects, avoiding MMI's and MDI's. AI CDSS's holds incredible promise to transform rational use of medication prescribing in the health care sector. AI's predictive analytics and ability to interpret large amounts of data can inform preventative care strategies, improve safety and quality control measures. Notwithstanding great advancements, artificial intelligence still has some limitations, but its opportunity is limitless, as there is still tremendous potential for consecutive research in the medical and dental fields to enhance safety and quality of healthcare.

The next frontier in research encompasses computational prediction models and artificial intelligence algorithms that could foresee MMI's and MDI's by accessing centralized pharmacology databases using internationally validated tools. The health care profession is set to change as AI technologies brings major benefits. However, ethical guardrails need to be in place to prevent risks associated with biases, discrimination, confidentiality, safety, transparency and responsibilities. Although AI can assist the medical and dental fields in many ways, still, the final decision must be made by the professional as the overall treatment is a multidisciplinary approach.

References

The full list of references 1-131 is available from:
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