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Medication errors in elderly people: contributing factors and future perspectives

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1. Older people have substantial interindividual variability in health, disability, age-related changes, polymorbidity, and associated polypharmacy, making generalization of prescribing recommendations difficult.
2. Medication use in older adults is often inappropriate and erroneous, partly because of the complexities of prescribing and partly because of many patient, provider, and health system factors that substantially influence the therapeutic value of medications in aged people.
3. A high prevalence of medication errors in older adults results on the one hand from accumulation of factors that contribute to medication errors in all age groups, such as polypharmacy, polymorbidity, enrolment in several disease-management programmes, and fragmentation of care. On the other hand, specific geriatric aspects play a role in these medication errors; these include age-related pharmacological changes, lack of specific evidence on the efficacy and safety of medications, underuse of comprehensive geriatric assessment, less availability of drug formulations offering geriatric doses, and inadequate harmonization of geriatric recommendations across Europe.
4. The dearth of geriatric clinical pharmacology and clinical pharmacy services compounds the difficulties.
5. There are gaps in research and clinical practice that lead to frequent medication errors in older adults, which must be solved by future studies and by regulatory measures in order to support errorless and appropriate use medications in these people.

According to the United Nations' Initiative of 1999, all nations should prepare their healthcare, social, and economic systems for recent and future demographic ageing of their populations [1]. Older people are rapidly increasing in number throughout the world, in both developed and developing countries, and among this age group multiple chronic and degenerative disorders are highly prevalent. Clinicians are spending larger proportions of their time in the management of drug dosage regimens in older adults, and knowledge of geriatric prescribing, clinical pharmacology, and clinical pharmacy has become essential in daily clinical practice. Nevertheless, there is a lack of specialists in geriatrics, clinical pharmacy, and particularly clinical pharmacology [2].

There is growing evidence of efficacy of therapeutic agents in older adults and increasing use of pharmacological interventions, effective marketing strategies, and self-medication. All of these factors contribute to increasing use of medications by older people, a high prevalence of polypharmacy, and consequently a high prevalence of medication errors. In the European project AgeD in HOme Care (ADHOC), polypharmacy (defined as nine and more medications) was reported by 22% of older adults (65+) in home care in Europe. In four of eight European countries the prevalence exceeded 20% (Finland 41%, the Czech Republic 39%, Iceland 32%, and the UK 20%) [3].

It is necessary to ensure effective and safe but cost-effective use of medications and good quality of life in older citizens. Studies from the USA have shown that suboptimal drug use and medication errors have an important impact on health and the national economy [4, 5]. However, lack of similar evidence in Europe contributes to underestimation of this problem in many European countries.

Here we summarize the gaps in geriatric research and clinical practice that lead to frequent medication errors in older people, which must be solved in future studies and by regulatory measures in order to support errorless and appropriate use of medications in these people.

Explicit tools for reducing prescribing errors in older patients

Older patients, who have complex clinical problems and take multiple treatments, are particularly susceptible to medication errors. They may, of course, have a genuine

Table 1

Some advantages and disadvantages of implicit and explicit methods for screening medications for appropriateness

Implicit methods	Explicit methods
Advantages	
• **Allow flexibility in individual patients**	• Consistency of approach to individual cases
• **Do not require problems to be prespecified**	• Can be adapted to computerized systems
	• Can incorporate information from published literature and expert consensus
	• Can easily be used for educational purposes, drug utilization reviews, and epidemiological studies
Disadvantages	
• **Depend on knowledge, experience, and skills of healthcare professionals**	• Do not allow flexibility in individual patients
• **More difficult to use consistently**	• Can produce false-positive results
• **More difficult to measure outcomes in valid and reliable ways**	• Need problems to be prespecified
	• Miss some problems that may be identified only during a full assessment of the patient

need for more medications; however, they are often victims of a 'prescribing cascade', have increased risks of drug–drug and drug–disease interactions, and often suffer inappropriate use of medications [6].

Among methods for identifying hazardous drugs in older patients, Beers' criteria have been the most commonly used in clinical practice and research in the past decade. In the USA, since 1991, Beers and colleagues have developed a set of explicit criteria for identifying inappropriate drugs, defined as medications in which the risk of use in elderly people substantially outweighs the benefit [7–9]. The original lists developed by Beers and Fick were adopted by Canadian authors in the form of McLeod's criteria [10] and by Laroche *et al.* in the form of a French consensus panel list of potentially inappropriate medications [11].

Beers' criteria were for many years regarded as the gold standard for assessing potentially inappropriate prescribing in older patients. However, there are several limitations to their use [12]: for example, they pay no attention to the role of the patient (including non-adherence to therapy and patients' willingness to accept risks of harm in return for benefits), and they do not pay systematic attention to various aspects of the treatment process; for example, the appropriateness of a medication may vary with the reason for prescribing it (such as neuroleptic drugs in patients with psychoses compared with patients with dementia) or in individual patients with different susceptibility factors for adverse drug reactions (including patients who have or lack specific genetic polymorphisms). Some of the medications on the lists that have been prescribed as inappropriate through the application of Beers' criteria may have acceptable indications in old people. Conversely, the lists are not without omissions – other substances with similar potentially inappropriate properties in elderly people are widely available in Europe (e.g. flunitrazepam and atypical antipsychotic drugs in high doses) [3, 12, 13]. Furthermore, more complex, explicit, criterion-based process measures are available [13]. It is widely accepted that Beers' criteria should not be applied indiscriminately.

Many authors emphasize that more up-to-date, systems-based, comprehensive screening tools are necessary for appropriate review of medications in elderly people [12, 13], and newer explicit instruments have been introduced in order to reduce the number of prescribing errors, including Screening Tool of Older Person's Prescriptions and Screening Tool to Alert doctors to Right Treatment [14]. However, it is necessary to emphasize that none of these explicit tools can fully substitute for comprehensive clinical and pharmacological review of medications, and both explicit and implicit methods must be rationally combined in individualized drug treatment [12, 13].

Explicit methods for reviewing medications are usually developed from published reviews, expert opinions, and consensus techniques. They can be applied with little or no clinical judgement and are mostly drug-oriented or disease-oriented. On the other hand, the focus of implicit methods is more on the individual patient than on the drugs or diseases, and clinicians have to use information from the patient and published studies to make individual judgements. These approaches are potentially the most sensitive, but they are time-consuming and can have poor reliability. They depend highly on clinicians' knowledge, skills, and attitudes [12, 15]. The advantages and disadvantages of implicit and explicit methods have been reviewed [15] and are summarized in Table 1.

Rational decisions in the use of drugs in older people – availability of evidence

Physicians who take care of elderly people should integrate their individual clinical expertise with the best external evidence and comprehensive information on the patient's disabilities, prognosis, preferences, predicaments,

family support, and costs of treatment [16]. In integrating external evidence or guidelines with good clinical skills, knowledge of geriatric pharmacology must be implemented, in order to decide what is most appropriate for the individual patient.

The border between rational and irrational drug use in geriatric medicine is narrow, and decisions are often complicated by lack of evidence or at least adequate evidence in older patients. As stated by Godlovitch, 'seniors often take medications in the absence of evidence about their efficacy and safety in higher age groups or are denied potentially effective treatments because medications are untried in their age group' [17]. Studies conducted in young individuals cannot always be extrapolated to older subjects, even with the use of detailed knowledge of applied geriatric pharmacology and pharmacoepidemiology and with the use of estimates of the changed therapeutic value of drugs because of other factors (such as polymorbidity, polypharmacy, poor adherence to therapy, disability).

The organizers of the European project Increasing PaRticipation of the ElDerly In Clinical Trials (PREDICT) summarized 5280 articles published before February 2008 (357 potentially relevant) in a systematic review [18]. They confirmed that the mean age of participants in clinical trials was much lower than that of real-life users of medications. In trials in heart failure, the mean age of participants was 61–63 years, but the common age at diagnosis was 74–78 years. In trials in Alzheimer's disease, the mean age of subjects was <75 years, but the incidence of the disease rises substantially over that age. Despite the fact that the prevalence of depression is highest in old people, only 9–11% of clinical trials of antidepressant treatments included older adults. In many clinical trials, comorbidities constituted frequent exclusion criteria. Recent evidence on the effectiveness and safety of medications therefore underestimates the needs of elderly people, who in many cases constitute the majority of users.

The main reasons for excluding older subjects from clinical trials included: medical factors (the high risk of adverse effects or a belief that the benefit of a drug was limited to a specific patient group); scientific factors (omitting older subjects because they are more likely to be lost to follow-up or in an effort to select a relatively homogeneous study sample); and medical or socioeconomic patient factors (compromised care, fear of the risks of treatment, difficulties with transport to a study centre, time conflicts, responsibilities of several physicians for prescribed medications, no direct interest of a patient in a clinical trial) [18, 19].

No reasonable justification for excluding older adults from clinical trials was documented in 35–78% of studies [18]. There is a gap to be filled in order to obtain better evidence for future treatment of older patients. The way forward is not only to overcome psychosocial and economic barriers of patients and professionals, but also to involve substantial numbers of geriatric pharmacologists and geriatricians in designing and evaluating clinical trials and to reduce unjustified exclusion of older adults by ethics committees solely on the basis of their age.

Recommendations for drug use in older people – the need for European harmonization

One of the current principal aims of the European Union is to improve practice, rules and regulations throughout the continent. As part of this aim, prescribing for older people should be improved and basic geriatric recommendations should be harmonized. Currently, there are substantial differences among geriatric guidelines and geriatric practices in different European countries, and prescribing for older people is strongly influenced by differences in drug policies, feedback strategies, and national drug formularies.

The organizers of the European project ADHOC have analysed the use and availability of potentially inappropriate medications in older adults undergoing home care in eight European countries (the Czech Republic, Denmark, Finland, Iceland, Italy, the Netherlands, Norway and the UK) [3]. Using a list derived from a combination of several explicit criteria (Beers' criteria [8], Fick's criteria [9] and McLeod's criteria [10]) they confirmed that the percentage of approved medications in national drug formularies varied across Europe, from 32% in Norway to 71% in Italy. Whereas certain potentially inappropriate medications were not available in some national formularies (e.g. pentoxiphylline in Norway, the Netherlands, Denmark, Iceland and the UK; belladonna alkaloids in Italy; hyoscyamine in Iceland), in other countries they were available but used only rarely (e.g. belladonna alkaloids, hyoscyamine, and pentoxiphylline in Finland and Italy) or available and used frequently (e.g. pentoxiphylline in the Czech Republic – 20% of users). Overall the prevalence of use ranged from 5.8% in Denmark to 41% in the Czech Republic and reflected differences in national drug formularies, country-specific drug policies, regulatory measures, care provision differences, and inequalities in the health and socioeconomic status of older people. Major recommendations related to the appropriate use of medications (including indication, dose, length of treatment, risk modifiers) should be harmonized across Europe.

Several studies in older people have confirmed that prescribing habits (local and country-specific) along with behavioural and socioeconomic factors (including prescribing limits, reduced access of older adults to safer treatments, disability, and inability or unwillingness to co-pay for safer alternatives) substantially contribute to inappropriate use of medications and higher costs [3, 20]. Since financial resources, patients' characteristics, and behavioural factors strongly influence geriatric prescribing, it is necessary to harmonize clinical recommendations,

produce national drug policies, and implement effective measures in Europe (e.g. to establish prescribing limits for ineffective or harmful medications in older patients, to approve safer alternatives, and to make low-dose drug formulations available economically for older adults) [3]. These strategies could improve prescribing for older people in the European Union.

Multidimensional geriatric assessment – providing individualized geriatric care and new geriatric evidence

Modern pharmacoepidemiological research in geriatrics should focus on well-designed outcome-oriented studies, with the use of huge, comprehensive, trans-national databases, in order to obtain valid information on outcomes of interventions and technologies (both pharmacological and nonpharmacological) in geriatrics. Such efforts could partly supplement information on the effectiveness and safety of different drugs and procedures derived from clinical trials [21].

The interRAI corporation international collaborative network of researchers and clinicians from over 30 countries worldwide (http://www.interrai.org) has developed standardized and validated Resident Assessment Instruments (RAI) for different settings of geriatric care, such as home care, long-term care, and acute care. These tools are used in many countries in geriatric practice and research [22–24].

InterRAI instruments provide an option for reliably determining a valid data set of key characteristics of older people (demographic, socioeconomic, clinical characteristics, and diagnoses), contemporaneous treatment strategies (including comprehensive drug information), care-related information, and selected measures of functional age, with validated geriatric scales embedded in the instrument [25].

InterRAI instruments are important for geriatric practice, in which multiple problems, diagnoses, drugs, and assessments are major risk factors for medication errors. Older people admitted to different care programmes often pass through a number of transition points in the same setting and between different healthcare professionals. The use of similar interRAI instruments in various settings enables the standardized documentation of major patient-related characteristics and information about socioeconomic status and care provision. This helps in reducing errors and medication errors.

The use of InterRAI tools in different countries worldwide has already had an important positive effect on individualized geriatric care and treatment, and their powerful role in cross-sectional and outcome geriatric research has been confirmed.

Conclusion

Reducing the rate of medication errors is a challenging task in geriatric patients, owing to the high prevalence of risk factors, the lack of sufficient evidence on the efficacy and safety of medications, and the many health system factors that contribute to the risks (e.g. several prescribing physicians responsible for the treatment of a single patient, inadequate continuity of care, and the low availability of clinical pharmacology and clinical pharmacy services).

Older people require particular attention from healthcare professionals, care planners and managers, and economists. Global evaluation of their needs and problems, including comorbidity, polypharmacy, disability, nonadherence and cognitive impairment, is necessary in order to reduce the risk of medication errors and appropriately weight the chances of benefit, the risks of harm, and the cost-effectiveness of drug treatments.

Future research and regulatory measures should focus on specific evidence in older patients; harmonization of clinical recommendations, drug policies, guidelines, and feedback strategies across Europe; implementation of comprehensive geriatric assessment; and increased availability of clinical pharmacology and clinical pharmacy services.

Competing interests

None to declare.

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